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"In Appraising Legislation Intended to Protect Public Health or Prevent Fraud, It Is Not Enough to Inquire Whether the Abuses Aimed At Are Likely to Be Cured; Political and Social Consequences Need to Be Envisaged Also."—Carl L. Alsberg.

Vol. XXIV, No. 3 MARCH, 1935

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 83rd ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN PORTLAND, ORE., AUGUST 5–10, 1935.

Local Secretary, A. O. Mickelsen, N. E. 6th Ave. at Oregon St., Portland, Ore., Hotel Multnomah, Headquarters.

The 1935 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Portland.

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E. F. KELLY, Secretary,
2215 Constitution Ave.,
Washington, D. C.

1935 MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The week of August 5th–10th has been named for the coming eighty-third annual convention of the AMERICAN PHARMACEUTICAL ASSOCIATION to be held in Portland, Ore. Headquarters will be the Multnomah hotel. A. O. Mickelsen is the Local Secretary and inquiries about the convention should be addressed to him, care of the North Pacific College of Pharmacy, Portland, Ore.

This is the first time the A. PH. A. will convene in the Pacific Northwest, but it has met before on the Pacific coast—once in Los Angeles and twice in San Francisco. Since this organization is the mother of all pharmaceutical associations of the country and draws its membership from all branches of pharmacy, it is expected that the coming conventions will draw large delegations from all sections.

The Mt. Hood Loop Highway, which marks a conquest of man, starts from Portland's doors; circles Mt. Hood towering 11,225 feet into the heavens. The

Mt. Hood in Oregon as seen from the Loop Highway which completely encircles the mountain; the round trip of 175 miles from Portland may easily be made in one day. The mountain itself is practically in Portland's front yard, being only 60 miles due east. Permission to use in JOURNAL A. PH. A. by *Sawyer Scenic Photos, Inc.*

world-famed Columbia River Highway starts eastward from the very edge of Portland. It was at Champoeg, a little spot on the Willamette 30 miles above Portland, that a provisional government of the Oregon country under the Stars and Stripes was declared on May 2, 1843. At the mouth of the Columbia River a hundred miles from Portland lies Astoria, the first settlement (1811), in Oregon. A few miles beyond lies Seaside, where Lewis and Clark reached the end of the trail. Just across the Columbia from Portland stand Vancouver Barracks, where General Grant and others of his day served as lieutenants and captains. Monuments, statues and shrines mark these places.

A feature of the convention week is the fact that the Oregon, Washington and Idaho State pharmaceutical associations will hold a big tri-state meeting in Portland on August 5th–6th, and it is expected that many of the delegates to this tri-state meeting will remain to participate in the deliberations of the A. PH. A. group. Further details of these conventions will appear in later issues of THIS JOURNAL.

ANTON HOGSTAD, JR.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXIV MARCH, 1935 No. 3

THE CHAIRMAN, NATIONAL PHARMACY WEEK EXECUTIVE COMMITTEE.

Anton Hogstad, Jr., Chairman, National Pharmacy Week Executive Committee was born February 21, 1893, in Neenah, Wisconsin. He graduated from the Philadelphia College of Pharmacy in 1914, being awarded the Clement B. Lowe Materia Medica Prize and the Henry Kraemer Microscopical Prize. Following graduation he remained at his Alma Mater for a period of two years in the Department of Botany and Pharmacognosy, after which he became associated with the former H. K. Mulford Company, in charge of the Hay Fever Department at the Glenolden Laboratories.

In 1917 he was called to the South Dakota State College Division of Pharmacy where he remained for a period of eight years, during which time he inaugurated the Medicinal and Poisonous Plant Garden, as well as engaging in an extensive piece of research involving the origin, physiological rôle and production of Oil of American Wormseed. During 1925–1926 he was the D. F. Jones Fellow in the Biochemical Division, University of Minnesota, continuing his studies in Biochemistry, Colloidal Chemistry and likewise Pharmacology.

In 1926 he was chosen to succeed the late Dr. Henry M. Whelpley as professor of Physiology and Materia Medica at the St. Louis College of Pharmacy, and was at that time appointed Pharmacognosist to the Missouri Botanical Garden, at which institution he inaugurated and developed their present medicinal plant garden.

Five years later he entered the retail field, establishing a well-known prescription shop in St. Louis which experienced an unprecedented success, the success of same being due in a large measure to the unusual methods adopted in rendering members of allied professions a distinct type of professional service.

On January 1, 1931, he became associated with Merck & Co., Inc., in the capacity of Special Assistant to the President, with instructions to render American Pharmacy every assistance possible. Upon the death of the late Dr. Robert J. Ruth, Mr. Hogstad was appointed chairman of the National Pharmacy Week

Executive Committee. During the course of the past four years he has traveled extensively, lecturing at Colleges of Pharmacy, local, state and national gatherings throughout the United States and Canada, as well as assisting retail pharmacists by rendering a distinct type of personal service.

On June 30, 1920, Mr. Hogstad was married to Ebba Henrietta Nesseth at Menomonie, Wisconsin; they have four children. Mr. Hogstad is keenly interested in the native medicinal plants. He is the founder of the St. Louis Wild Flower Club. He is also vitally interested in Colloidal Chemistry. For four years he addressed the St. Louis Colloidal Medical Club monthly on Colloidal Chemistry in relation to Medicine.

PRELIMINARY NOTICE FROM THE COMMITTEE ON TRANSPORTATION.

Members attending the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in Portland, Oregon, August 5th–10th, will have an opportunity to visit the great west at moderate expense and under unusually favorable conditions. The Committee on Transportation is working with the railroads and steamboat companies to the end that members will be able to take advantage of very low summer excursion rates to the coast which will allow a wide choice of routes, going out by any one of many routes and returning by any other, including the whole length of California, Oregon and Washington, either from the north or the south.

In making arrangements for transportation, the Committee is endeavoring to leave the widest possible latitude of choice to the members, who may stop over at the Grand Canyon, or Yellowstone Park, or any of several other places; and several tours to Alaska will be available at the end of the meeting. Professor Gathercoal, the Chicago member of the Committee, is organizing a special tour from Chicago to the convention, with a stop over at Glacier National Park, and returning through the Canadian Rockies, which members from other sections will be welcome to join. More detailed information on transportation arrangements will be given in later notices from the Committee.—T. J. BRADLEY, *Chairman*.

ABSTRACT SECTION OF THE JOURNAL.

Beginning with this issue of the JOURNAL Pharmaceutical Abstracts will be published in a section near the end of the text pages in 32-page forms. The latter are paged consecutively so that they can be taken out of the JOURNAL and bound at the end of the year. Those who desire may also purchase duplicate forms or obtain bound copies of them.

If a sufficient number of laboratories or individuals desire reprints of the Abstracts, arrangements may be made for furnishing them. Replies should be mailed promptly to the Editor, 2215 Constitution Ave., Washington, D. C.

The Abstracts replace those of the YEAR BOOK and as they are published soon after the articles appear in the pharmaceutical publications, it is hoped that they will add to the service given by the ASSOCIATION. "The Bibliography of Pharmaceutical Research" heretofore published at the conclusion of the Scientific Section will be discontinued.

PAPERS FOR THE SECTIONS OF PORTLAND A. PH. A. MEETING.

Members of the AMERICAN PHARMACEUTICAL ASSOCIATION who contemplate presenting papers at the Portland meeting are referred to page 172 of the February JOURNAL for the names and addresses of officers of the Sections. In sending papers, carbon copies may be addressed to the JOURNAL, 2215 Constitution Ave., Washington, D. C.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

INTERNATIONAL CONGRESS OF PHARMACY.

AS stated in February JOURNAL the International Pharmaceutical Federation has selected Brussels for the twelfth International Congress of Pharmacy, July 30th to August 5th, coinciding with the Exposition Universelle of 1935. The Congress is under the patronage of King Leopold III. The program of the Congress details the entire domain of pharmaceutical subjects: Galenic pharmacy, pharmaceutical chemistry, analytical chemistry, toxicological chemistry, bromatology, pharmacognosy, microbiology, bacteriology, hygiene, history of pharmacy. The Secretary-General is Pharmacist J. Breugelmans, 3 rue du Gouvernement Provisoire, Brussels. Those who will attend should advise the latter promptly, giving title and profession, title of paper and advise whether it will be illustrated and whether experiments will be made during presentation. Only those articles will be accepted which are received prior to May 30th, as they are to be printed in advance of the meeting of the Congress. The official language of the Congress is French, but reports and communications may be written in any other language.

The Scientific Committee is composed of Prof. A. Castille, University of Louvain; Prof. A. J. J. Van de Velde, University of Ghent; Prof. F. Schoofs, University of Liège; Pharmacist O. Van Schoor; Prof. N. Wattiez, University of Brussels. The secretaries are: E. Delvaux, University of Louvain; H. Lecocq, A. Gilkinst Institute of Pharmacy, University of Liège. The Professional Interests Section is presided over by G. van de Vorst, of the Societé de Pharmacie d' Anviers. M. Breugelmans is the editor of *Journal de Pharmacie de Belgique;* the February 17th number contains a complete program of the Congress, part of which includes the entertainment features and information relative to trips that may be taken by visitors. It is hoped that visitors from the United States will arrange their travels for attendance at the meeting.

PAN-AMERICAN MEDICAL ASSOCIATION.

THE sixth congress of the Pan-American Medical Association will hold its sessions on board the steamship Columbia, sailing from New York on August 28th. The itinerary includes Havana, Curaçao, Trinidad, Santo Domingo, Jamaica, Rio de Janeiro, Santos and Sao Paulo in Brazil. The activities of the Association represent all branches of medicine, including studies on the United States and pharmacopœias of other American Republics. The Association has provided an award for post-graduate study; this year's selection will be made by the medical profession of Brazil.

The session of 1933 was held in Dallas, Tex., at which time Theodore J. Bradley presided over the Pharmacopœial Section. Chairman E. Fullerton Cook,[1] U. S. P. Revision Committee, presented a plan for coöperation, embodying general principles for an effort to reach an agreement on standards, pharmacopœial uniformity, contacts with the Health Departments of the Republics represented,

[1] JOUR. A. PH. A., 22, 456 (1933).

pharmacopœial information, and to agree upon the adoption of suitable titles and synonyms, and uniform strengths and percentages of purity.

The general plans of this year's congress were made March 1st, in New York City at a dinner in honor of Dr. Oswaldo Aranha, Brazilian Ambassador to the United States. The possibility of valuable results through coöperation of the divisions of medicine in the American Republics is evident, but systematic and persistent encouragement is essential.

DIVISION OF HEALTH SCIENCES.

THE regents of the University of Michigan at their meeting in January established a Division of the Health Sciences, which is to consist of the Medical School, the School of Dentistry, the Division of Hygiene and Public Health, the University Hospital School of Nursing, the College of Pharmacy and Post-Graduate Education. The purpose of this new division is to coördinate the work of all the divisions of the University which are concerned with the public health sciences, and the committee of this division is to act in an advisory manner.

The faculty of the College of Pharmacy considers that this step is a clear recognition on the part of the regents of the University of the importance of pharmacy as one of the public health sciences.

DRUG JARS IN NEW YORK MUSEUM.

THE interest of collectors in drug jars is shown in the exhibition at the American Art Association—Anderson Galleries of the collection of the late John Wanamaker. The latter display was in the home of Mr. Wanamaker on shelves which have been brought to the Museum; the containers are traced back to the Middle Ages and were made at the great pottery works of that period, such as Urbino, Castle Durante and Faenze, in Italy, and important centers in France, Holland and Spain.

Associated with the collection referred to are other specimens, mortars and pestles; some of the bronze mortars show "the interest of the time in ornamenting every day objects." Walter Rendell Storey writes interestingly on the subject in the *New York Times Magazine* of March 3rd, in an article wherein descriptions are given of the jars and mortars, now sought by collectors because of their ornamentation and ceramic importance.

DANISH REVIEW OF "PROFESSIONAL PHARMACY."

Svend Nielsen has published an extensive review of "Professional Pharmacy" prepared by Frank A. Delgado and Arthur A. Kimball, under authority of the U. S. Department of Commerce, Daniel C. Roper, *Secretary*, Bureau of Foreign and Domestic Commerce, Willard L. Thorp, *Director*.

This review appeared in the *Farmaceutisk Tidende* and is reprinted as a booklet. It affords the Danish pharmacists an opportunity to acquaint themselves with American pharmaceutical activities and exhibits the interest of Dr. Svend Nielsen in the subject. The authors are honored by the recognition and the AMERICAN PHARMACEUTICAL ASSOCIATION appreciates the value placed on the publication by the pharmacists of Denmark.

It may be stated here that the first edition of "Professional Pharmacy" is exhausted and a revision with considerable important additional matter is in preparation.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins, George D. Beal, L. W. Rising, H. M. Burlage, L. W. Rowe, John C. Krantz, Jr., Heber W. Youngken.

THE ACTIVE CONSTITUENTS OF ERGOT.

A PHARMACOLOGICAL AND CHEMICAL STUDY.

BY MARVIN R. THOMPSON.

(*Concluded from January* JOURNAL A. PH. A., *page 38.*)

THE CHEMICAL ISOLATION OF A HITHERTO UNIDENTIFIED MEMBER OF THE "TOTAL SPECIFIC ALKALOIDS" OF ERGOT.

It was believed, after many unsuccessful attempts in various directions, that the most fruitful procedure to follow in attempting to isolate the new promptly acting alkaloid would be to obtain the total alkaloids in as pure a condition as possible, and then to remove all of the alkaloids having the slow ergotoxine or ergotamine type of activity, leaving the promptly acting new alkaloidal principle or principles uncontaminated as far as the known alkaloids are concerned. This proved to be a successful procedure.

Since the "Total Alkaloidal Fraction" was completely clear and colorless, and since pharmacologic tests had shown this material to contain essentially every trace of the significant activity of the drug, this activity residing wholly in the "total alkaloids" as tartrates, this solution provided an excellent starting point. Accordingly 1 Kg. of defatted Ergot was worked up to this point in the previously described manner. This colorless acid aqueous solution was then again alkalinized and exhaustively shaken out with many small portions of ether. The Smith colorimetric test and pregnant cats were extensively used to follow the extractions to prevent loss of alkaloids. As usual, all operations were carried out in the dark to prevent oxidation of these labile substances. The ethereal solution was then taken to complete dryness *in vacuo*, first over $CaCl_2$, then over P_2O_5, without heat.

This dry amorphous total alkaloidal residue could be purified and freed from most of the known inert (ergotinine, ergotaminine) or "orally slow acting" alkaloid (ergotoxine and/or ergotamine (?), etc.) in a number of ways because of the observation that the new alkaloidal substance, either in the form of the free base or its corresponding salts such as sulphate, phosphate, hydrochloride, tartrate, etc., was found to be far more soluble in all of the common organic solvents (methyl and ethyl alcohol, ether, chloroform, acetone, benzene, carbon bisulphide, carbon tetrachloride) than any of the four well-known alkaloids. Especially remarkable was the observation that the new alkaloid was somewhat soluble in water even as the free base, in marked contrast to ergotoxine or ergotamine. Separation of the "orally slow acting" ergotoxine or ergotamine type of alkaloid from the "orally quick acting" new alkaloid could therefore be accomplished either by: (*a*) Dissolving the above total alkaloidal residue in anhydrous ether, converting the alkaloids to their corresponding sulphates causing a precipitation of most of the "orally slow-acting" alkaloids which settle out in an over-night period, leaving the "orally quick-acting" new alkaloid in solution, or, (*b*) Dissolving the total alkaloidal residue in acetone, and cautiously adding water until precipitation of the ergotoxine or ergotamine type of alkaloid was complete, with subsequent removal by filtration, leaving the new alkaloid in solution.

By either procedure, the filtrate contained the new "orally quick-acting" alkaloidal substance, which was obtained in an amorphous condition upon removal of the solvent *in vacuo*. In two trial lots, this amorphous alkaloid was purified further by redissolving the material in 0.5% aqueous tartaric acid and taking advantage of the observation that partial saturation with sodium bicarbonate causes precipitation of the new alkaloid from concentrated solutions. The substance

was then collected upon a filter in the dark, and promptly dried in a desiccator *in vacuo*. Working with 1 and 2 Kg. quantities of ergot, the yield was 176 mg. and 221 mg. of alkaloid per Kg. of original ergot, respectively, indicating that the percentage yield is increased when larger lots of the drug are used.

CHEMICAL NATURE OF THE NEW ALKALOIDAL SUBSTANCE.

The new substance has not been obtained in a chemically pure completely crystalline condition. Quantitative data, therefore, will not be given at this time.[1] The approximately quantitative information which follows is presented solely because of the important bearing the results of this report have, *first*, upon the clinical observations of Moir pointing to a new important non-alkaloidal constituent in Ergot, and *second*, upon the suitability of currently used methods of assay and standardization for U. S. P., B. P. and other Pharmacopœial preparations of this drug.

The new alkaloidal substance contains all of the elements contained in ergotoxine (10), ergotamine (11), ergotinine (12), and ergotaminine (11), namely, C, H, O and N. The proportions of these elements likewise have been found to roughly approximate those of the known alkaloids in a single analysis of the (impure ?) material. The figures are withheld pending further analyses upon material of known purity, but it may be stated that this analysis indicates that the molecule of the new alkaloid is definitely smaller than that of either ergotoxine, ergotinine, ergotamine or ergotaminine.

It is insoluble in petroleum ether, but definitely more soluble in water, ethanol, ether, benzene, methanol, the chlor-ethylenes and the chlor-methanes, than the known alkaloids. It appears in representative, but variable, amounts in all freshly prepared liquid extracts such as Fluidextract of Ergot, U. S. P., and Liquid Extract of Ergot, B. P. It likewise appears in powdered and pilular extracts, such as "Ergotin" or Aqueous Extract of Ergot, N. F. V, in extremely variable amounts, depending largely upon the amount of heat employed in the manufacturing

TABLE II.—ALKALOIDS OF ERGOT.

No.	Alkaloid.	Discoverer and Year Reported.	Composition (Supposed).	Oxytocic Activity Following Oral Administration.	Van Urk (19) or Smith (3) Color Reaction.	Cockscomb and Isolated Rabbit Uterine (2) Reaction.
1	Ergotinine (12)	Tanret (1875)	$C_{35}H_{39}O_5N_5$ (Barger)	Negligible	Positive	Negligible
2	Ergotoxine (10)	Barger and Carr (1907)	$C_{35}H_{41}O_6N_5$	Delayed but somewhat active on cat and human	Positive	Powerful
3	Ergotamine (11)	Stoll (1920)	$C_{33}H_{35}O_5N_5$	Delayed but somewhat active on cat and human	Positive	Powerful
4	Ergotaminine (11)	Stoll (1920)	$C_{33}H_{35}O_5N_5$	Negligible	Positive	Negligible
5	Pseudo-ergotinine (13)	Smith and Timmis (1931)	$C_{35}H_{41}O_6N_5$ (assigned with reservation)	Unknown (probably inert)	Positive	Negligible (?)
6	Sensibamine (14)	Wolf (1931)	$C_{31}H_{37}O_5N_5$	Unknown	Positive	Powerful
7	Ergoclavin (15)	Küssner (1934)	$C_{31}H_{37}O_5N_5 \cdot H_2O$	Unknown	Positive	Powerful
8	"X alkaloid"	Thompson (1934)	C H O N (mixture (?)) formula not yet assigned	Promptly and highly active on cats and humans*	Positive	Powerful

* See appended note at end of article.

[1] This amorphous "X alkaloid" has very recently yielded a crystalline product. Pharmacological and chemical studies upon these crystals are being pursued. Precise qualitative and quantitative data may, therefore, be presented in a later report.

process. Boiling temperatures gradually destroy the alkaloid in aqueous medium, but the destruction is usually far from complete after many hours, especially if partial vacuum is coincidently employed to affect concentration of the extract. Concentration of extracts in metallic vessels, with heat *in vacuo* or otherwise, markedly accelerated the destruction of this active substance as well as the other alkaloids.

The new alkaloid is much more stable than the ergotoxine type of alkaloid in crude extracts (either liquid or solid). Oxidation, spontaneous or chemically induced, causes the substance to become yellow, and finally a dark brown. This oxidation is attended by a corresponding decline in oxytocic activity.

Tested colorimetrically by the Smith method, or as modified by the 1932 B. P., the blue color was readily obtained. Of five different lots prepared to date, the intensity of the color reaction ranged from approximately 30% (for the less purified material) up to 60% (for the more purified material) of that produced by equivalent concentrations of ergotoxine ethanesulphate.

It is of interest at this point to consider the possible identity of the new alkaloid, and its possible relationship to the four well-known alkaloids, as well as some alkaloidal substances which have been obtained and described by others since 1931. These alkaloids, exclusive of substances known to be degradation products of the alkaloids, with their discoverers, etc., may be tabulated as in Table II.

It will be observed from Table II that all of the known alkaloids are closely related chemically. They can be distinguished from one another, however, by differences in solubility, optical rotation, melting points (especially their crystalline salts which generally melt more sharply than either the crystalline or amorphous bases themselves), ease of crystallization, crystallizing medium, and character of crystals, but the very practically important and readily utilizable method of distinguishing between them is to be found in the promptness of their pharmacological and clinical activity following oral administration.

Alkaloids Nos. 1 and 4 may be at once dismissed as unimportant because they are practically inert even upon the isolated uterus. No. 5 probably falls in the same class, because of its extremely close relationship to the inactive ergotinine (13). They are pharmacologically inert, thereby differing in the main essential from Nos. 2, 3, 6, 7 and 8. Nos. 2, 3, 6, 7 and 8 all appear to be pharmacologically active when tested upon the isolated rabbit uterus or other hitherto widely employed pharmacologic methods. Nos. 2 and 3, however, differ greatly from No. 8 in that the oxytocic response following oral administration to pregnant cats is much more prompt and effective for No. 8 than for Nos. 2 and 3. As to Nos. 6 and 7, nothing can be said from the standpoint of promptness or effectiveness when given orally, since they were not available for this study, nor has any such information been made available by others. Regarding No. 6, Barger (16) stated that Stoll had challenged the claim that this was a new alkaloid, because upon mere recrystallization ergotamine was obtained. (Note chemical similarity between 6 and 7.) As to the relationship existing between Nos. 7 and 8, it can only be stated that they are both highly active upon the isolated rabbit uterus, they appear to be similar as to solubility, both being water-soluble, but whether No. 7 exhibits the prompt oral activity of No. 8 is unknown. None of No. 7 was available for this study because of the fact that the report by Küssner (15) was obtained just prior to the sending of this report to press.

PHARMACOLOGIC ACTION OF THE NEW ALKALOID.

(*a*) *Upon the Cockscomb.*—The U. S. P. Cockscomb method measures this alkaloid along with the ergotoxine or ergotamine present in ergot preparations. 0.2 to 0.4 mg. per Kg. consistently produced definite cyanosis of the combs.

(*b*) *By the Epinephrine-Inhibition Isolated Rabbit Uterus Method* (*2*).—The purest of the five lots prepared to date acted in a manner qualitatively indistinguishable from ergotoxine or ergotamine. Quantitatively, the new substance appeared to be slightly more than half as potent as ergotoxine, in its possibly contaminated amorphous state.

(*c*) *Upon Carotid Blood Pressure of Anesthetized Cats and Dogs.*—Injected intravenously, a pressor action was demonstrated upon both cats and dogs, the effects upon the two species being similar. An example of this activity is shown in Fig. 10. The pressor effect was also similar to that of either ergotoxine or ergotamine by the intravenous route.

The "vasomotor reversal" was readily produced in two cats, as illustrated in Fig. 10-*a*. Repeated dosage produced gradually diminishing pressor response until doses similar to the first effective dose would no longer produce an effect.

Oral doses up to 1 mg. produced no significant change in carotid blood pressure of cats during one hour.

(*d*) *Upon the Isolated Uterus of the Guinea Pig.*—These effects, using immature virgin uteri, were likewise indistinguishable from those of the "Total Alkaloidal Fraction," already described.

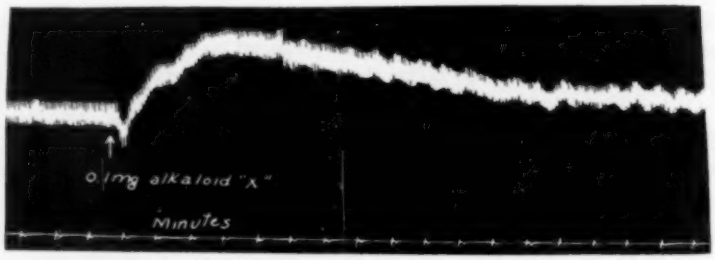

Fig. 10.—Male cat: 2.9 Kg.: Dial-urethane anesthesia: carotid blood pressure. The pressor response following the intravenous administration of 0.1 mg. of "X alkaloid."

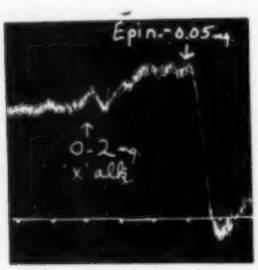

Fig. 10-*a*.—Male cat: 3.1 Kg.: Dial-urethane anesthesia; carotid blood pressure, illustrating the "vasomotor-reversal" induced by the "X alkaloid." Minutes.

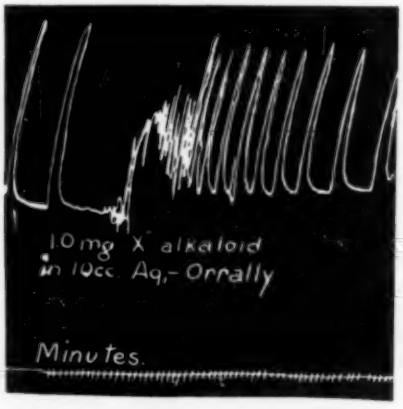

Fig. 11.—Cat: late pregnancy, uterus *in situ*. The prompt response following the oral administration of 1.0 mg. "X alkaloid," with 10 cc. of water.

Following the method previously described by the author (7), using mature uteri, histamine response was effectively inhibited in a manner similar to that produced by ergotoxine, ergotamine or the "Total Alkaloidal Fraction."

(*e*) *Upon Normal Unanesthetized Pregnant Cats.*—Either oral (1.0 mg.) or subcutaneous (0.5 mg.) doses were consistently effective in terminating pregnancy in a total of 21 cats in various stages of pregnancy. The young were invariably dead at birth. Death of two cats resulted after abortion, following a subcutaneous dose of 1.0 mg. to each, but this dose was not always fatal.

(*f*) *Upon the Uterus of the Lightly Anesthetized Pregnant Cat.*—This was the only pharmacologic method which clearly revealed a difference between the new alkaloid and ergotoxine or ergotamine.

Recording the movements of the uterus of the pregnant cat *in situ*, in the usual manner, oral doses of 1.0 to 2.0 mg. of the new alkaloid in 10 to 20 cc. of water have been observed to produce a uterine response usually well within five minutes, rarely beyond ten minutes, in 17 experiments.

Corresponding doses of ergotoxine or ergotamine, as shown earlier in this report, are active in causing a response, but never in less than twenty minutes (usually thirty minutes or more). An example of the prompt response is illustrated in Fig. 11. The activity is of long duration. Experiments have been observed up to four hours at which time evidence of activity had not ceased to be apparent.

SUMMARY AND CORRELATION OF RESULTS.

The uterine activity of various "type" extracts of ergot and commercially available salts of ergotoxine and ergotamine has been studied by observing the effects following oral, subcutaneous and intramuscular administration to anesthetized and unanesthetized cats in the later stages of pregnancy.

The method involving the recording of the uterine movements of the pregnant cat *in situ* provided a means of pharmacologically demonstrating an important difference between ergotoxine or ergotamine, and crude aqueous or hydroalcoholic extracts of ergot, confirming Moir's clinical observations on this point. These studies have also confirmed Moir's conclusion that there exists in ergot a highly important new "as yet unidentified substance" in ergot.

Contrary to Moir's apparent belief, however, the present studies have shown that all of the activity obtained from his various ergot preparations, could have been obtained from no constituents of ergot other than one or more of the "total alkaloids." Even in the case of his "Aqueous Extracts," which are admittedly deficient in ergot alkaloids, the present studies have demonstrated that all of the significant activity shown by these preparations could have been due to no substances other than "residual alkaloid."[1]

[1] In a recent lecture (November 14, 1933) on ergot in London by Professor G. Barger (16), the lecturer discussed, among other things, the clinical observations of Moir pointing to a new important non-alkaloidal principle in ergot. "The lecturer stated that this was also his own opinion up to about three months ago, when he thought that that was the situation. One U. S. worker, Marvin Thompson, who has published some accurate estimations of Ergot varieties, had raised doubts in his mind as to whether the action was not, after all, due to some residual alkaloid. He would like to say very little on the subject, and he put forward the suggestion with some hesitation." The discussion provoked by Prof. Barger's lecture was also published by the same *Journal* (16). This discussion was very interesting to the present writer, inasmuch as the comments were made by a number of workers who have been most active in this field, including Dr. Moir, Sir Henry Dale and Professor Burn. It is quite obvious, from the comments made by these workers, that they had little faith in the contention of "the American worker" that the activity observed by Moir from Aqueous Extracts was due to "residual alkaloid." Professor Burn stated that "it was difficult to see how 'residual alkaloid' could produce an effect in a patient, either quicker or as quickly as any other physiological effect." Dr. Moir stated, in part, that "The point was that an 'inactive' preparation proved to be active," obviously implying that an alkaloid-free preparation was clinically active. Sir Henry Dale stated, among other things, that "With regard to his (Professor Barger's) statements, referring to work in America, which suggested that the action was due to residual alkaloid, he did not believe it. He thought that the amount of residual alkaloid was quite trivial."

Replying to these comments, the present writer refers the reader to the evidence of this report, including the appended note. It was this evidence which was discussed with Professor Barger during his visit in Baltimore, and which caused him to make mention of the matter in his lecture. In the studies reported by Moir, it is believed that the prompt and impressive activity he obtained from all of his extracts was due to ergot alkaloids. Although he assumed his aqueous extracts to be essentially alkaloid-free, assays of numerous such extracts by the present writer have usually shown them to contain an alkaloidal content of 0.05 to 0.20 mg.

A chemical procedure for completely separating ergot into its "total alkaloidal" and "non-alkaloidal" fractions has been described. The colorless "Total Alkaloidal Fraction" has been found to contain all of the significant oxytocic activity of the drug, while all of the remaining constituents of ergot contained in the "Alkaloid-free" fraction were found to be completely devoid of any valuable oxytocic activity.

The "Total Alkaloidal Fraction" was observed to exhibit oxytocic activity in a manner superior to that of ergotoxine or ergotamine, proving that the "Total Alkaloidal Fraction" contained at least one hitherto unknown alkaloid.

A chemical procedure has been described for fractionating the "total alkaloids" by removing the ergotoxine, ergotamine, ergotinine and ergotaminine, leaving the new alkaloidal substance in solution. A method for the purification and isolation of the new substance in amorphous condition likewise has been presented. This substance, as it was obtained for these studies, was not proved to be a pure chemical entity, but was highly active.

The new alkaloid was found to differ pharmacologically from the hitherto known active alkaloids mainly in the promptness of its oxytocic action, especially following oral administration. The action of the new alkaloid usually developed in one to ten minutes, while the action of ergotoxine and ergotamine developed in twenty-five to sixty minutes, following oral administration of large doses to pregnant cats. Hitherto available methods (blood pressure, cockscomb, isolated tissues, etc.) failed to significantly distinguish qualitatively between ergotoxine or ergotamine and the new alkaloid. This is undoubtedly the reason for the hitherto well-established, although erroneous, opinion among pharmacologists that either ergotoxine or ergotamine were completely representative of the total activity of the drug or its extracts.

The results make it appear that the chief important differences between the new "X alkaloid" and the well-known ergotoxine or ergotamine are that the former is more soluble and more rapidly absorbable than either of the latter alkaloids. Little, if any difference is evident upon blood pressure following *intravenous* administration, or when compared upon *isolated* smooth muscle. It should be emphasized, however, that while the two types of alkaloid act similarly upon *blood pressure* following intravenous administration, the activity upon the *uterus in situ*, by the same route, is by no means similar. The activity of the new alkaloid is definitely more prompt and pronounced than that of ergotoxine or ergotamine, although the difference is not as great as when both types of alkaloid are given orally. It would appear, therefore, that the effect of either upon blood pressure is almost immediately dependent upon the concentration in the blood stream, but that the uterine effect is produced only after some further absorption or diffusion from the blood stream, perhaps into the lymphatic circulation, before exerting an effect upon the uterine innervation.

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per cc. in terms of either ergotoxine or ergotamine. Since Moir administered doses of such extracts ranging from 4.0 to 16.0 cc., it should be observed that the alkaloidal equivalent of such doses would range somewhere between 0.2 and 3.2 mg. The present writer has found that the greater part of the total alkaloids of aqueous extracts consists of the new alkaloid instead of ergotoxine or ergotamine, because of the greater ease of extraction and greater stability of the new alkaloid. Interpretation of Moir's results in the light of the results of this study, shows that the oxytocic effects he obtained from even his aqueous extracts were certainly due to "residual alkaloid," and this consisting principally of the new alkaloid here described.

It has been demonstrated that the active principles of ergot (total alkaloids) are not absorbed from the stomach of the cat, and that absorption occurs only after passage through the pylorus into the intestine. It is believed that this is probably likewise true in humans because of the fact that the time for onset of action from a given active preparation is not absolutely constant for different patients (see appended note, also Moir's results). Administration of the oral dose with 10 to 20 cc. of water causes a much more consistently prompt response in cats, than when the same dose is given without water, presumably due to a more prompt opening of the pylorus stimulated by the larger bulk of fluid.

Aqueous and hydro-alcoholic extracts, when injected subcutaneously or intramuscularly, were observed to be intensely irritant. In the large doses, huge, slow-healing abscesses were produced. This is not an uncommon experience with clinicians. The severe irritation and abscesses have been shown to be caused, not by the valuable colorless (in solution) oxytocic constituents of ergot, but by the difficultly absorbable, deeply colored, inert fraction. The presence of these difficultly absorbable inert constituents in injectable ergot preparations should be condemned.

Hydro-alcoholic types of liquid extracts of ergot, when freshly and properly prepared, have been shown to contain all of the "total alkaloids" of the drug. They are, therefore, completely representative of the drug itself, as far as oxytocic activity is concerned. They are suitable for oral administration only, because they contain the irritant and difficultly absorbable inert constituents, and are, therefore, prone to cause pain and abscesses upon hypodermic injection.

Aqueous types of liquid extracts of ergot do not contain all of the "total alkaloids" of the drug. They have been found to contain practically all of the promptly acting new "X alkaloid," but only insignificant amounts of the slow acting ergotoxine or ergotamine type of alkaloid. Although the promptly acting "X alkaloid" is the more important because of its prompt action, the slow-acting ergotoxine or ergotamine type of alkaloid is, nevertheless, significantly active, undoubtedly adding considerably to the duration of effect. Such preparations, therefore, cannot be regarded as being completely representative of the drug. They are suitable for oral administration only, because they contain the irritant and difficultly absorbable inert constituents, and are, therefore, prone to cause pain and abscesses upon hypodermic injection.

The value of solid or pilular extracts (ergotins) for oral administration depends entirely upon the type of procedure used in their manufacture, particularly with respect to the amount of heat used. They can be prepared so as to be highly active, and if physiologically standardized, should be dependable. Most of such extracts available at the present time have had much of their alkaloidal activity destroyed by the excessive heat used in their manufacture (from the examination of 37 commercial samples, the manufacturing process of which was precisely known by the writer for 19 of the samples), and practically none of them is standardized. They owe the greater part of any activity they possess to the new "X alkaloid."

The currently available methods of assay and standardization have been studied with reference to their value in insuring activity in ergot preparations, and their relative merits discussed. The U. S. P. Cockscomb method, the Broom-Clark Rabbit Uterus method, the Thompson Histamine-Inhibition Guinea-Pig

Uterus method, and the Smith colorimetric method, with the various modifications of each, have been shown to measure the new alkaloid along with the ergotoxine or ergotamine type of activity, but none of these methods can readily serve to distinguish between the prompt-acting new alkaloid and the slow-acting ergotoxine or ergotamine type alkaloid as these alkaloids exist in official extracts. Inasmuch as the new alkaloid is extracted easier, and appears to be much more stable than the ergotoxine or ergotamine type alkaloid (as these alkaloids exist in Pharmacopœial ergot preparations), it is believed that the use of any one of the above methods can be applied in such a manner as to insure satisfactorily standardized amounts of activity in such extracts. The method should, therefore, be chosen from the standpoint of routine reliability and precision. From this standpoint, the author favors a modification of the Broom-Clark Rabbit Uterus method (2), but has become favorably impressed with the merits and possibilities of the Colorimetric method. These methods will receive more specific consideration in a separate communication.

All of the above methods require the use of a "standard of comparison." The writer has examined all of the only four lots of U. S. P. Standard Fluidextract ever prepared and distributed by the U. S. Department of Agriculture. Nos. 635, 636 and 2160 have been shown to be unstable in an earlier report (17). The last lot prepared and distributed, No. 2835, has been observed to lose not less than half of its original activity from the time it was first tested, in July 1932, until last tested in January 1934. This standard, therefore, fails in its purpose.

The author (18), in 1930, recommended that either ergotoxine ethanesulphonate[1] or ergotamine tartrate be adopted as the bioassay standard in place of the faulty "U. S. P. Standard Fluidextract." These two salts have now been employed by the writer for over five years in testing ergot preparations. Both have been found to be satisfactory from the standpoint of stability. Since the newly discovered alkaloid shows a type of activity which is measured by all of the assay methods enumerated above, being practically indistinguishable from ergotoxine or ergotamine by such methods, and since a preparation of the new alkaloid of proven stability cannot be available for at least several years, it is believed that the adoption of one of the alkaloidal salts previously recommended is a virtual necessity. Until more appropriate methods of assay are available, a perfectly stable salt of the new alkaloid would have no advantage over available ergotoxine or ergotamine salts as a bioassay standard of comparison. In the light of evidence to date, including Moir's observations upon humans, the observations set forth in this report, and the studies by Koff upon humans (see appended note), the relationship existing between quantitative bioassay results (U. S. P. or other methods measuring "total alkaloidal activity") may be illustrated by taking a properly prepared representative U. S. P. Fluidextract of Ergot as containing all of the therapeutically active principles of the drug. Arbitrarily assigning the value of 100% to both the clinical activity and the bioassay (cockscomb, etc.) activity, the new "X alkaloid" is present in such proportions as to account for 15 to 25% of the bioassay activity, but owing

[1] The ergotoxine ethanesulphonate used in these studies was very kindly supplied by Dr. Clifford S. Leonard, Burroughs Wellcome & Co. For the generosity in supplying the ergotamine tartrate and methanesulphonate here employed, the author is indebted to The Sandoz Chemical Works.

to the great clinical effectiveness of this alkaloid, it accounts for approximately 75% of the clinical activity. The slow and feebly acting (clinically) ergotoxine or ergotamine type of alkaloid in such a fluidextract accounts for 75 to 85% of the bioassay activity, but only 15 to 25% (approx.) of the clinical activity. The "X alkaloid" is extracted much more easily and is more stable than the ergotoxine type of alkaloid. Therefore, a fluidextract may assay as low as 15 to 20% of U. S. P. requirements and still retain the greater part of its clinical oxytocic activity.

CONCLUSIONS.

1. The pregnant cat has been found to be a suitable test subject upon which to study comparatively the oxytocic activity of various types of preparations and constituents of ergot.

2. A procedure, involving oral administration of the ergot preparations, has been described and used extensively for the above purpose. Such a procedure can be successfully employed in investigating the chemical source of the significant oxytocic activity of ergot.

3. Carefully prepared hydro-alcoholic extracts of ergot, such as Fluidextract of Ergot, U. S. P. (U. S. P. X or Interim Revision), or Liquid Extract of Ergot, 1932 B. P., contain all of the important active principles of the drug. Such preparations are rich in alkaloids and are remarkably prompt and effective upon the uterus following oral administration.

4. Aqueous extracts of ergot do not contain all of the important active principles of the drug. They are deficient in ergot alkaloids, but are never alkaloid-free unless they are many years old or the alkaloids have been destroyed by excessive heat in their manufacture. When carefully prepared, these extracts are remarkably prompt and effective upon the uterus following oral administration. This prompt and effective activity is entirely out of proportion to the ergotoxine or ergotamine equivalents of such preparations.

5. Ergotoxine and ergotamine are indistinguishable in producing a much delayed and erratic action following oral administration. The activity of these alkaloids is, therefore, far from being completely representative of the drug itself or its crude extracts, as formerly supposed.

6. A hitherto unknown, highly important, active principle exists in ergot.

7. Every trace of the significant oxytocic activity has been found to reside in the chemically purified "total alkaloids" of the drug, even in the so-called aqueous extracts, as shown by the prompt activity obtained from the "Total Alkaloidal Fraction" in contrast to the complete lack of significant activity in the "Alkaloid-Free Fraction."

8. Ergotoxine and ergotamine are not representative of the "total alkaloidal activity." The new active principle appears, therefore, to be another member of the specific alkaloids of ergot, since it followed the other alkaloids in the chemical procedure used in obtaining the "Total Alkaloidal Fraction."

9. The activity of aqueous extracts observed by Moir must have been due, contrary to his belief, to "residual alkaloid" consisting mainly of the new alkaloid described in this report. The alkaloidal deficiency of such extracts is due to the inefficiency of water in extracting the ergotoxine or ergotamine. Most of the more

stable new alkaloid is readily extracted by water and hence appears in fairly representative amounts in such extracts.

10. The new alkaloid has been isolated in a sufficiently pure amorphous condition to permit of certain pharmacological and chemical comparisons with the hitherto known alkaloids.

11. The new alkaloid is closely related to ergotoxine and ergotamine as is shown by similar chemical behavior and also as is shown by its similar pharmacological action when tested upon the isolated guinea-pig uterus, the isolated rabbit uterus, the cockscomb and the carotid blood pressure of cats or dogs. Its activity persists for hours, as does that of ergotoxine and ergotamine.

12. The new alkaloid differs from ergotamine and ergotoxine mainly by its much more soluble nature, and by its more prompt and powerful oxytocic action following oral administration. The greater solubility, together with the probability that the new alkaloid has a smaller molecule, compared with ergotoxine or ergotamine, undoubtedly accounts for the more prompt absorption and greater effectiveness of the new alkaloid.

13. All of the remarkable observations of Moir can be explained by the demonstration of the existence of the new alkaloid.

14. None of the active oxytocic principles of ergot (the specific alkaloids) are absorbed to any significant extent from the stomach of the cat, following oral administration.

15. All of the active oxytocic principles of ergot (the specific alkaloids) are absorbed with varying degrees of rapidity from the intestine of the cat following oral administration. The new alkaloid is promptly absorbed while ergotoxine and ergotamine are absorbed with great difficulty. This difference in absorption rate also manifests itself following subcutaneous or intramuscular injection.

16. Ordinary aqueous or hydro-alcoholic extracts of ergot are intensely irritant to the tissues following subcutaneous or intramuscular administration. Severe abscesses develop at the site of injection, especially following the larger doses.

17. The irritant and abscess-forming properties are not due to the important active principles (the specific alkaloids) of ergot. They are due to the otherwise pharmacologically inert extractives appearing in the liquid extracts.

18. The color of an ergot preparation is no indication of its value or activity. The purified, total active principles are colorless in solution.

19. Either ergotoxine ethanesulphonate or ergotamine tartrate constitutes the best available "standard" for comparison in the evaluation of ergot preparations by the currently accepted quantitative methods.

20. The Isolated Guinea-Pig Uterus method, as usually applied (as in testing Liquor Pituitarii, U. S. P.), is wholly unreliable as a means of insuring significant activity in ordinary aqueous or hydro-alcoholic extracts. It measures chiefly the worthless non-specific amine activity of such extracts.

21. Clinical activity in reasonably standardized amounts can be insured by requiring official liquid ergot extracts to contain a total specific alkaloidal activity, equivalent to approximately 0.05 per cent, in terms of either ergotoxine ethanesulphonate or ergotamine tartrate, when tested by the Cockscomb method, the Epinephrine-Inhibition Rabbit Uterus method or the Colorimetric method. This will provide for the presence of essentially all of the more important new alkaloid

present in the parent drug, plus varying but larger proportions of the less important ergotoxine or ergotamine. None of these methods can serve to differentiate between the new alkaloid, ergotoxine or ergotamine in crude extracts.

22. Solid or pilular extracts can be made to contain a satisfactory amount of activity by extracting properly and avoiding the use of excessive heat and exposure to oxygen in the process of concentration.

23. The non-specific amino-bases of ergot (histamine, tyramine, cholines, etc.) contribute nothing of a desirable nature to the characteristic oxytocic activity of the drug.

NOTE ADDED MAY 1, 1934.

Through the kindness of Dr. Arthur K. Koff, Woman's Clinic, The Johns Hopkins Hospital, some clinical confirmation of the pharmacological and chemical evidence of this report has been obtained. During the past two years, Dr. Koff has conducted over fifty experiments upon human patients, recording the oxytocic action of drugs in a manner essentially similar to that employed by Dr. Moir in England. After observing the clinical response of different ergot preparations, he has, among other things, confirmed Dr. Moir's observations that both the aqueous and alcoholic types of crude extracts, given orally, cause a remarkably prompt and intense uterine response, entirely out of proportion to their ergotoxine or ergotamine equivalent, and that oral doses of salts of ergotoxine and ergotamine produce only a much delayed and feeble response even in very large doses.

Upon being informed of the pharmacological and chemical results obtained by the author, Dr. Koff very kindly agreed to observe the activity of certain preparations upon human patients, recording the uterine contractions directly as in Moir's experiments. The author's "Alkaloid-Free Fraction," freshly prepared as described in the above report, except that 1 cc. represented 2 Gm. instead of 1 Gm. of ergot, administered orally to three patients, proved to be completely inert in doses up to 10 cc., representing 20 Gm. of the original ergot. The original fluidextract, from which the "Alkaloid-Free Fraction" was prepared, produced the characteristic prompt and pronounced effects of the crude extracts upon these same patients, in 4-cc. doses (representing 4 Gm. ergot), the effect developing within fifteen minutes in every case.

An oral dose of 4.0 cc. of "Total Alkaloidal Fraction," prepared as described in the above report, and representing 4.0 Gm. of the original ergot, administered to one patient, produced a pronounced effect well within fifteen minutes. The promptness of action was indistinguishable from that produced by the fluidextract from which both "fractions" were prepared. The effect was still pronounced after nine hours, observations being discontinued at this point.

The orally "slow-acting" ergotoxine or ergotamine type of alkaloid, separated in the usual described manner from the "Total Alkaloidal Fraction," proved to be devoid of the prompt type of activity following an oral dose of the alkaloid equivalent to 8 Gm. of the original ergot to one patient. No effect whatever was evident for more than an hour, after which a feeble effect, entirely similar to that produced by available salts of ergotoxine and ergotamine, was produced.

These clinical experiments are especially significant because of the fact that the difference between the delayed and erratic ergotoxine or ergotamine effect and the prompt action of crude extracts is so great and so consistent that it is quite unnecessary to carry out numerous experiments in order to show the difference. It will be noted that these experiments upon humans have confirmed the results obtained upon the pregnant cat in every case. The "Alkaloid-Free Fraction" was capable of producing no oxytocic effect upon cat or human. The "Total Alkaloidal Fraction" produced a prompt and intense oxytocic effect upon both cat and human. The ergotamine or ergotoxine type" of alkaloid removed from the "Total Alkaloidal Fraction" produced a much delayed feeble effect upon the human and the cat (huge doses to cats produce an intense effect, but it is always much slower in developing than in the case of the crude extracts or the "Total Alkaloidal Fraction"), entirely similar to that produced by commercially available salts of ergotoxine and ergotamine.

The details of these clinical experiments will be more completely described elsewhere by Dr. Koff.

The author wishes to acknowledge indebtedness to Professor E. V. McCollum, School of Hygiene and Public Health, The Johns Hopkins University, for his inspirational guidance, and to express sincere appreciation for his constant encouragement during this investigation.

He also wishes to express gratitude to Professors J. J. Abel, E. K. Marshall and E. M. K. Ceiling, Department of Pharmacology of the Medical School, The Johns Hopkins University, and Professor G. Barger, University of Edinburgh, for helpful criticism and valuable suggestions, and to Dr. Arthur K. Koff of the Woman's Clinic, The Johns Hopkins Hospital, for extending invaluable clinical coöperation.

Full responsibility is assumed by the writer, however, for any errors in presentation, results or conclusions which may appear in this report.

REFERENCES.

(1) Thompson, JOUR. A. PH. A., 22, 736 (1933).
(2) Thompson, *Ibid.*, 21, 1135 (1932).
(3) Smith, *U. S. Pub. Health Rep.*, 45, 1466 (1930).
(4) Moir, *Brit. Med. J.*, June 4th, 1022 (1932).
(5) Moir, *Ibid.*, June 18th, 1119 (1932).
(6) Thompson, JOUR. A. PH. A., 19, 705 (1930)
(7) Thompson, *Ibid.*, 18, 1106 (1929).
(8) Thompson, *Ibid.*, 19, 11 (1930).
(9) Thompson, *Ibid.*, 19, 221 (1930).
(10) Barger and Carr, *Chem. News*, 94, 89 (1906).
(11) Stoll, *Schweiz. Apoth. Z.*, 60, No. 26 (1922).
(12) Tanret, *Compt. rend.*, 81, 896 (1875).
(13) Smith and Timmis, *J. Chem. Soc.*, 1888 (1931).
(14) Chinoin, A. G., and Wolf, Brit. Pat. No. 388,529 (1931).
(15) Küssner, *Arch. Pharm. Ber. Deut. pharm. Ges.*, 3, 503 (1934).
(16) Barger, *Pharm. J.*, Nov. 18, 597 (1933).
(17) Thompson, JOUR. A. PH. A., 20, 1027 (1931).
(18) McClosky, Thompson and Barbella, *Ibid.*, 19, 844 (1930).
(19) Van Urk, *Pharm. Weekblad*, 66, 473 (1929).

SOME PHARMACOLOGICAL AND BACTERICIDAL PROPERTIES OF UMBELLULONE.*,1,2

BY MILES E. DRAKE[3] AND ERNST T. STUHR.

INTRODUCTION.

The literature on the oil of the California laurel, *Umbellularia californica* (Hook. and Arn.) Nutt., includes very little information on the pharmacology of the oil, or of the ketone (umbellulone) obtained from it. Likewise, no reference was

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* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] An abstract based upon a thesis by Miles E. Drake submitted to the faculty of the Graduate School of the Oregon State College, in partial fulfilment of the requirements for the degree of Master of Science in Pharmacy.

[2] Department of Pharmacology and Pharmacognosy, School of Pharmacy, Oregon State College.

[3] Fairchild Scholar, 1933.

found in the literature on volatile or essential oils in regard to the germicidal or fungicidal activity of this oil and ketone. Extensive research has been pursued on the chemistry of the constituents in this oil by various investigators.

Persons who have come in close proximity with the myrtle oil or its vapors report discomforts, such as severe headaches, irritation of the skin and mucous membrane, and in several instances unconsciousness resulted. The apparent potency of the oil prompted this investigation.

HISTORICAL.

Umbellularia californica (Hook. and Arn.) Nutt. was first collected in California by Menzies (1) in the latter part of the eighteenth century. Prior to Menzies, the Spaniards of California knew the tree as *Laurel Silvestre.*

In 1826 Douglass (2) classified this evergreen tree as a laurel, *Laurus regia* (the regal laurel) probably intending to indicate the beauty and splendor of the tree.

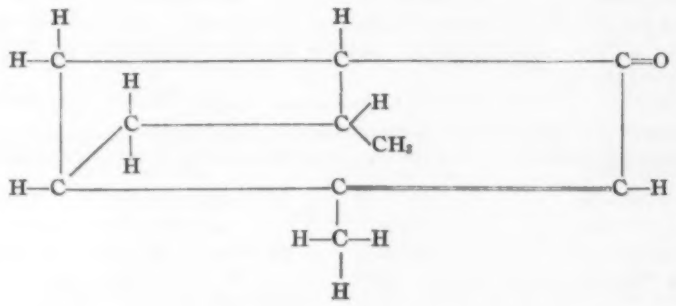
Fig. 1.—Myrtle Tree (*Umbellularia californica*).

In 1833 Hooker and Arnott (3) classified this evergreen as *Tetranthera californica*. Later Nuttal (3) gave it the present name of *Umbellularia californica*. As far as has been reported this is the only representative of the genus *Umbellularia*.

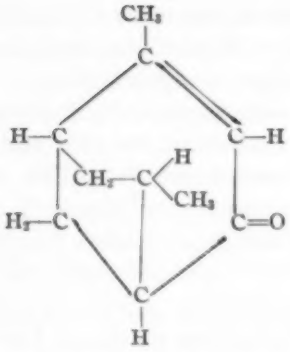
Heaney (4) in 1875 by fractionation under reduced pressure obtained from the oil of the California laurel a colorless liquid (Oreodaphenol) possessing a pungent odor.

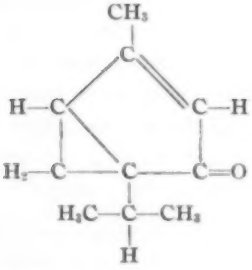
Stillman (5) in 1880 by fractionation at 215–216° C. obtained a colorless mobile liquid possessing an aromatic but pungent odor. Excessive inhalations of the vapors of this fraction were observed to produce headaches.

Powers and Lee (6) in 1904 reported the following principles or constituents which the oil yielded on fractionation: pinene, cineol, eugenol, methyl eugenol and a ketone, umbellulone, which was collected at 217–222° C. The purified ketone had a sp. gr. of 0.9584 at 15/15, $[\alpha]_D - 37°$ in a 100-mm. tube. Powers and Lee (6) concluded that umbellulone had one ethylenic linkage, and gave it the following structural formula:



Tutin (7) in 1908 gave umbellulone the following structural formula:





Semmller (8) in 1908 gave umbellulone the structural formula which is accepted to-day. According to Spiegel (9), sabinol, thujone and umbellulone are very similar in structure.

DISTILLATION AND DESCRIPTION OF THE OIL OF MYRTLE.

The leaves after drying are steam distilled. The oil is collected in an excess of water distillate which on standing separates into two layers, the oil layer being on top of the water layer. The layer of oil is decanted and dried over anhydrous sodium sulphate. The yield of the oil, according to Parry (10), varies from 2.5 to 5.5 per cent.

The oil of *Umbellularia californica* is a clear brownish yellow liquid. It possesses a sweet but pungent, irritating, empyreumatic, persistent odor. Parry (10) gives this oil a sp. gr. of 0.935 to 0.950, and an optical rotation of −22°. Sawyer (11) states that the dry oil has a sp. gr. of 0.936, and a solubility of 1:1000 in water.

THE KETONE FROM THE OIL OF MYRTLE.

Wienhaus and Todenhofer (12) in 1929 prepared the ketone, umbellulone, from the oil of myrtle by preparing a water-soluble sulphite addition product from the oil. This addition product was steam distilled and purified by fractionation under reduced pressure. Following the method of Wienhaus and Todenhofer no appreciable ketone yield was obtained; therefore, the following modified method was employed.

Method No. 1. Modified Wienhaus and Todenhofer.—Three hundred and fifty grams of myrtle oil were shaken out twice with a saturated solution composed of 400 Gm. of sodium sulphite and 80 Gm. of sodium bicarbonate in 400 cc. of distilled water. This solution when neutral to five drops of phenolphthalein was shaken vigorously for 30 minutes. The resulting mixture was allowed to separate and the oil layer was decanted. This oil was then treated with a second 400 cc. of the saturated sodium sulphite-bicarbonate solution and permitted to stand 24 hours. The oil was again decanted, and the aqueous portions of the first and second washings were combined and steam-distilled in a neutral condition for two hours in order to free the aqueous solution of any excess oil. The oil-free aqueous residue was treated with 40 Gm. of stick sodium hydroxide and the mixture was steam distilled for three hours. The resulting product was fractionated under 4-mm. reduced pressure, yielding purified umbellulone at 77.5–77.8° C. (uncorrected). Yield 48 Gm.

Physical Constants of the Ketone (Umbellulone).—$[\alpha]_{D21}$ −38.50; n_D 1.48285; $d_{28}°$ 0.9465, agreeing fairly well with the reports of Wienhaus and Todenhofer (12).

The following tabulation gives the constants reported by various investigators.

TABLE I.

	Sp. Gr.	Op. Act.	R. I.	B. P. 4 Mm.
Wienhaus and Todenhofer (12)	0.949 (20°)	−38.51	1.48315 (20°)	85°
Stillman (5)		−36.30		
Powers and Lee (6)	0.9614 (15.5°)	−36.33	1.18325 (20°)	
Authors	0.9465 (25°)	−38.50	1.48285 (20°)	77.5–77.8°

Method No. 2. Fractionation.—Three hundred grams of myrtle oil were fractionated at 4-mm. reduced pressure. A total of nine fractions was collected. Fraction IV (74–78° C.) and Fraction V (78–80° C.) were refractionated. Fraction No. 2 (77.1–77.6° C.) of IV, and fraction No. 1 (77.2–77.7° C.) of V were combined and refractionated, yielding 61 Gm. of the ketone, umbellulone at 77.1–77.7° C. Only two physical constants were taken of this fraction. The B. P. by the capillary method (13) was found to be 216–217° C. (corrected). The refractive index was found to be 1.4830 at 21° C. Yield: The following percentages of ketone yield were obtained:

Modified Wienhaus and Todenhofer method	13.71%
Fractionation method	20.3%

as compared to yields reported by previous investigators:

Wienhaus and Todenhofer (12)	24.5%
Powers and Lee (6)	60.0%
Stillman (5)	40.0%
Russell (14)	28.0%

SOLUBILITY OF UMBELLULONE.

Freely soluble in 70 per cent alcohol	Freely soluble in liquid petrolatum
Freely soluble in olive oil	Freely soluble in Miller solvent (19).

PRELIMINARY INVESTIGATION.

Effects on Blood in Vitro.—To determine the action of umbellulone on defibrinated blood *in vitro* the method of Dessemontit (15) was used. To one cc. of blood was added three cc. of 0.9% sodium chloride and 0.06 cc. of umbellulone. This mixture was warmed gently, placed in a Sedgwick counter and observed through a spectrometer. Horse blood and guinea-pig blood were used.

Results:

Diluted horse blood—no bands were present within range of methemoglobin.

Diluted horse blood plus 10% solution of potassium ferricyanide—upon heating gently the blood became a chocolate brown and the following bands were noted:

First Trial.		Second Trial.	
First band	635–631 μ μ	First band	636–632 μ μ
Second band	588–572 μ μ	Second band	587–572 μ μ
Third band	554–532 μ μ	Third band	544–532 μ μ

Diluted horse blood plus 0.06 cc. of umbellulone—upon heating the blood became a chocolate brown and the following bands were noted:

First Trial.		Second Trial.	
First band	635–631 μ μ	First band	634–631 μ μ
Second band	587–571 μ μ	Second band	589–573 μ μ
Third band	555–536 μ μ	Third band	554–532 μ μ

Diluted guinea-pig blood plus 0.06 cc. of umbellulone—the following bands were noted:

	First Trial.	Second Trial.	Third Trial.
First band	634–630 μ μ	634–631 μ μ	635–630 μ μ
Second band	586–572 μ μ	588–571 μ μ	589–572 μ μ
Third band	553–533 μ μ	553–534 μ μ	553–534 μ μ

The bands obtained on both horse blood and guinea-pig blood are in fair agreement with those reported by Halliburton (16). The center of the absorption band considered as characteristic had a wave-length of 630–634 μ μ, according to Dessemontit (15).

Effects on Blood in Vivo.—A guinea pig received two cc. of 1:1000 umbellulone in olive oil intraperitoneally three times a week for six weeks. At the end of six weeks the blood was obtained by the heart stab method and kept at 37.5° C. until used. To one cc. of this blood was added three cc. of 0.9 per cent sodium chloride solution. The results were as follows:

First band	634–630 $\mu\mu$
Second band	587–573 $\mu\mu$
Third band	554–532 $\mu\mu$

Figure 2 shows the absorption band at 630–634 $\mu\mu$. The guide lines above are the neon lines. (Page 203.)

Further work showed that umbellulone produced decided hemolysis of human, guinea-pig and horse blood.

Effects of Umbellulone upon the Intact Heart of the Frog.—The frogs were prepared for heart recording (17) and 0.2 cc. of 10 per cent umbellulone in 1 per cent acacia emulsion dropped upon the heart after a normal tracing had been obtained. Results:

Umbellulone at first produced a quickening in the heart rate which was followed by a progressive decrease in frequency, loss in tonus and a decrease in contraction of the ventricle. The heart finally stopped in diastole. It was found that the addition of 0.1 cc. of 1:1000 caffeine to the washed heart produced no reviving effect. The injection of 0.2 cc. of 1:1000 adrenaline hydrochloride into the right atrium also produced no reviving effect upon the paralyzed heart.

Effects of Umbellulone on the Atropinized Frog Heart.—The hearts of other frogs were first treated with 0.2 cc. of 1% atropine and the atropine allowed to take effect. About five minutes after the application of the atropine the excess was washed off with 0.65 per cent sodium chloride solution and 0.2 cc. of 10 per cent umbellulone dropped upon the heart. There was at first a quickening of the heart rate, which was followed by a progressive decrease in frequency, loss in tonus and a decrease in contraction of the ventricle. The heart stopped in diastole.

Effects of Physostigmine on Umbellulonized Frog Heart.—The hearts of frogs were treated with a 10 per cent solution of umbellulone. There was an initial increase of rate or frequency, followed by a progressive decrease in frequency, ending in apparent paralysis of heart. Several drops of 1:100 physostigmine solution were applied to the paralyzed heart, resulting in partial revival.

Effects of Umbellulone on Unanæsthetized Animals.—Injection:

Two guinea pigs were used, each receiving an intraperitoneal injection of four cc. of a 10 per cent solution of umbellulone in olive oil. Two minutes after the injection the guinea pigs showed a slight paralysis of the hind quarters. This was followed by a drop in pulse rate with a slight change in respiration which rapidly became very irregular. Both pigs showed asphyxia convulsions which became more frequent and pronounced toward the end of the experiment. Following the decrease in pulse rate there was a marked increase in the pulse which was followed by failure in respiration. The heart stopped in about a minute after respiration failure.

Post-mortem examination indicated the odor of umbellulone pronounced in both peritoneal and pericardial cavities. The heart stopped in diastole. The

heart, aorta and the superior and inferior vena cava were dilated. The lungs showed decided congestion and the blood was of a dark color.

Inhalation:

Warmed umbellulone was placed in a desiccator and allowed to vaporize in the presence of a guinea pig for a period of four hours. At intervals the enclosed chamber was oxygenated. The only apparent result was irritation of the mucous membranes of the eyes and nose. The respiration was at times irregular but at no time did it show signs of failure.

Experimental Work. I. Bactericidal Aspects.

Fungicidal action of the oil and the umbellulone.

Method:

The organisms used were *Monilia tropicalis* (1885) and *Trychophyton interdigetale* (2284).

The Food and Drug Administration method (18) was used with a standard loop for transferring to a broth of p_H 5.0 for a period of five days.

The solvent (19) employed to dissolve the ketone, umbellulone, was a sterilized mixture composed of 33 parts, respectively, of 95 per cent alcohol, glycerol, distilled water and 6.6 parts of powdered castile soap. This solvent was tested for fungicidal action and was found to check with the reports of Miller (19).

The fungicidal action of umbellulone was determined by a modification of the method by Kingery and Adkison (20). Two cc. of the ketone solution was placed in one cc. of 24-hour broth culture and allowed to stand for the specified intervals of time (one, thirty and sixty minutes), and then transfers were made to Sabouraud's Agar medium and incubated for 48 hours and read.

Ten experiments were undertaken. Table II is a tabulation of the typical results obtained.

Table II.

No.	Dilution.	Oil of Myrtle. Time in Minutes. 1.	30.	60.	Check.	Umbellulone. Time in Minutes. 1.	30.	60.	Check.
1885	1/10	−	−	−	++++	−	−	−	++++
	1/50	++	−	−	++++	−	−	−	++++
	1/100	++++	++	+	++++	+	−	−	++++
	1/1000	++++	+++	++	++++	++++	+	+	++++
2284	1/10	−	−	−	++++	−	−	−	++++
	1/50	+	−	−	++++	−	−	−	++++
	1/100	+++	++	+	++++	+	−	−	++++
	1/1000	++++	+++	++	++++	++++	++	++	++++

Legend to table:

−	No growth recorded.
+	1–4 colonies observed on the quarter.
++	5–10 colonies observed on the quarter.
+++	11–24 colonies observed on the quarter.
++++	25 or more colonies observed on the quarter.

The oil and the ketone in the absence of protein killed the specific organisms used in dilutions of 1:10 for intervals of 1, 30 and 60 minutes, but in a 1:50 dilution growth was recorded with one-minute contact for the oil of myrtle, but not for the umbellulone. In the 1:100 dilution there was recorded growth in all intervals of time for the oil of myrtle, while the ketone showed no growth on 60 minutes' contact. In 1:1000 dilution all contacts were positive.

The fact that the organisms were killed and not inhibited was demonstrated by taking a loop of each dilution for the various intervals of time, and transferring to a sterile tube of broth. No growth was recorded in 48 hours at 37° C.

FUNGICIDAL ACTION OF UMBELLULONE IN THE PRESENCE OF PROTEIN.

Fifteen experiments were undertaken.

Method:

Organisms (1885 and 2284) and the F. D. A. method (18) of transferring were used with the same technique as before, using media containing gelatin, peptone and 10 per cent defibrinated horse blood in Sabouraud's medium. The p_H for the respective media was adjusted to 5.5 and sterilized at 15 lbs. pressure for 18 minutes.

Results:

Blood Medium.—In the presence of 10 per cent blood medium, organism (1885) was killed for all contacts of time intervals by 1:10 dilution. 1:100 dilution was negative in 60-minute contact; 1:1000 dilution was positive in all contacts. The same results were recorded for organism (2284).

Gelatin and Peptone Media.—Organism (1885): All contacts were negative in 1:10 dilution; 1:100 dilution, 1-minute contact was positive, 30- and 60-minute contacts were negative; 1:1000 dilution, all the contacts of time intervals were positive.

Organism (2284): 1:1000 dilution on gelatin medium recorded positive in 1- and 30-minute contacts, while the 60-minute contact was negative. All other recordings were identical with those of organism (1885).

Umbellulone in the presence of protein-like materials was found to be only slightly inactivated.

NOTE: The dilutions as specified in all these experiments are as before adding to the 24-hour broth culture, in each case the original dilution was diluted one-half.

GERMICIDAL ACTION OF UMBELLULONE.

Method:

A. Wet Filter-paper method of the F. D. A. (18) was employed. Organisms used were *E. typhi* (Sears) and a standard stock culture of *Staphlococcus albus*. Neither organism was inhibited or killed by 5-minute exposures to 1:70 dilution of phenol. Both organisms were killed by a 15-minute exposure in a 1:90 dilution of phenol.

Results:

The accompanying Table III is typical of the results obtained.

TABLE III.

Organism.	Time.	Dilutions. 1:10	1:20	1:100	1:500	1:1000	1:2000
E. typhi	1	−	−	−	+	+	+
	2	−	−	−	+	+	+
	5	−	−	−	−	+	+
	7½	−	−	−	−	+	+
	15	−	−	−	−	−	+
	30	−	−	−	−	−	+
	60	−	−	−	−	−	+

Staph. albus	1	–	–	–	+	+	+
	2	–	–	–	+	+	+
	5	–	–	–	+	+	+
	7½	–	–	–	+	+	+
	15	–	–	–	–	+	+
	30	–	–	–	–	–	+
	60	–	–	–	–	–	+

Estimated phenol coefficient, 6.25.

B. The F. D. A. Agar-Plate Method (18).—E. typhi (Sears) and *Staph. albus* were the organisms used. The ointments were composed of: Umbellulone 10 per cent, 5 per cent, 1 per cent and 1:10 of one per cent, with lanolin as a base.

Results:

All dilutions showed inhibitory and diffusibility action. The fact that *E. typhi* and *Staph. albus* were killed was determined by using a portion of the material from the clear zone of the plate and transferring to sterile tubes of broth which were incubated for 24 hours at 37° C.

II. Effects of Umbellulone on Isolated Intestinal Segment.

The following experiments were carried out by using a modification of the procedure of Salant and Mitchell (21).

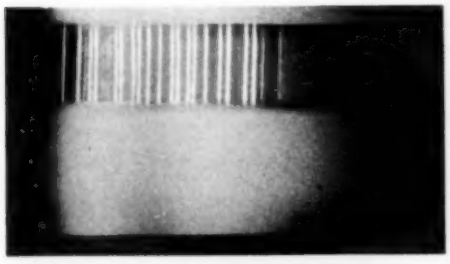


Fig. 2.—Spectrogram of the umbellulone on guinea pig blood.

Fig. 3.—Rabbit gut. Effect of 1 cc. of 1/100 solution of umbellulone, giving a dilution of 1–40,000. (A) Normal; (B) Partial paralysis; (C) Normal segment. Base line indicates two-minute intervals.

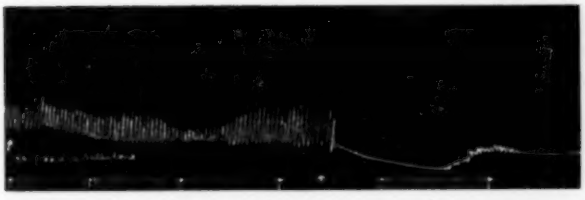


Fig. 4.—Rabbit gut. Showing progressive loss of contraction (in dilution of 1–13,333 of umbellulone), with period of slight stimulation and complete paralysis of intestinal segment. Time—two-minute intervals.

Fig. 5.—Rabbit gut. Intestinal segment revived in Locke's solution. Time—two-minute intervals.

Method:

The rabbits and cats were killed by administering an excessive dose of chloroform. The small intestines were immediately removed, care being taken to avoid injury to the intestines. The removed intestines were placed in fresh, oxygenated Locke's solution and kept at 37.5° C.

until used. The segments of the intestines (2.5 to 4 centimeters in length) were suspended in four hundred cc. of Locke's solution through which a stream of oxygen was bubbling continuously. The temperature was maintained at 37.5° C. by use of a constant temperature bath. Recordings were made on a single drum kymograph, using a Becker universal lever. The umbellulone was prepared in the form of a 1 per cent acacia emulsion. Dilutions of 1:10, 1:100 and 1:1000 were prepared for use in the experiment.

Results:

Both cat and rabbit gut when treated with a 1:100,000 dilution of umbellulone showed a slight stimulation with a slight increase in contraction, with tonus and amplitude remaining nearly constant.

Rabbit Gut.—Umbellulone in a dilution of 1:40,000 produced decided decrease in contraction (Fig. 3). In a dilution of 1:13,333 umbellulone produced a decided decrease in contraction, tonus and amplitude. This decrease was progressive in nature (Fig. 4). On washing gut with fresh Locke's solution the segment was revived (Fig. 5).

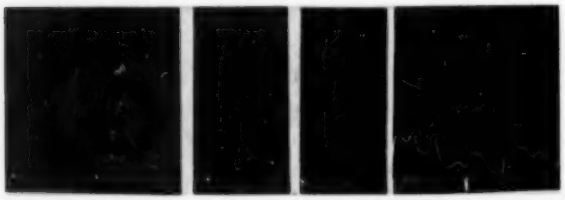


Fig. 6.—Cat gut. Effect of 1–5000 dilution of umbellulone on isolated intestinal segment. Time—two-minute intervals.

Cat Gut.—Umbellulone in a dilution of 1:5000 produced a progressive decrease in contraction, tonus and amplitude, finally resulting in paralysis of segment (Fig. 6). On washing gut with fresh Locke's solution the segment was revived.

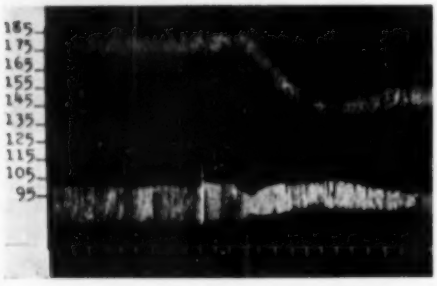


Fig. 7.—Dog. Blood-pressure and respiration. Normal B. P. from right carotid artery; normal respiration. Effects from femoral vein injection of 1 cc. undiluted umbellulone. Time—ten-second intervals.

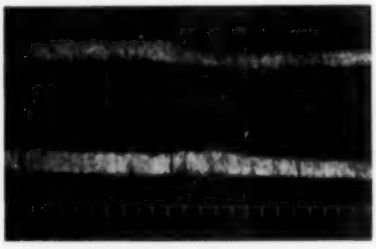


Fig. 8.—Dog. Blood-pressure and respiration. (Continuation of Fig. 7.) Progressive rise in B. P.; increased heart action; rapid (shallow) respiration, and intestinal stimulation. Time—ten-second intervals.

III. Effects of Umbellulone on Respiration and Blood Pressure.

Dogs were the only animals used in this work. A total of seven dogs was used.

Method:

The dogs were weighed and 1.2 cc. of 40 per cent chloretone in 40 per cent ethyl alcohol (22) per Kg. of body weight were injected intraperitoneally. Two and one-half hours later the dogs were prepared for blood pressure recording (23, 24) by using a Becker U tube mercury manometer for blood pressure and a Becker respiration plethysmograph for respiration. Both respiration and blood pressure were recorded on a single drum kymograph.

Results:

Umbellulone, when given intravenously, in a dose of 0.109 cc. per Kg. of body weight produced a rapid and decided fall in blood pressure (Fig. 7). This

Fig. 9.—Dog. Blood-pressure and respiration. (Continuation of Fig. 8.) Second femoral injection (1 cc. undiluted umbellulone). Effects—failure of respiration, and arrest of heart beat. Time—ten-second intervals.

was followed by a progressive rise in the blood pressure which at no time regained the mean pressure (Fig. 8). The injection of a second dose of similar size, as stated above, produced death in a few minutes with failure in respiration followed by arrest of the heart (Fig. 9).

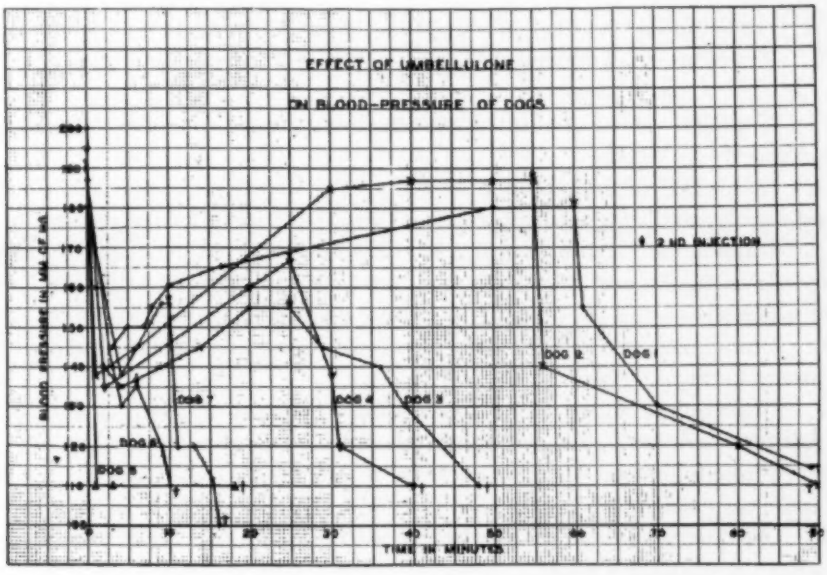


Fig. 10.

TABLE IV.—EFFECTS OF UMBELLULONE ON THE BLOOD PRESSURE AND RESPIRATION OF DOGS.

			10% Umbellulone in Olive Oil.				20% Umbellulone in Olive Oil.				Undiluted Umbellulone.				
			10 Cc. Injection.		10 Cc. Injection.		7 Cc. Injection.		7 Cc. Injection.		1 Cc. Injection.		1 Cc. Injection.		Death Resulted.
Dog.	Normal. Resp.	B. P.	Resp.	B. P.	Resp.	B. P.	Resp.	B. P.	Resp.	B. P.	Resp.	B. P.	Resp.	B. P.	Min.
1	40	200	24	140	3	110									89
2	37	195	22	138	4	110									90
3	27	192					18	135	23	110					48
4	35	195					21	138	25	110					40
5*	28	190									5	110			3
6	58	187									156	135	18	110	9
7	72	180									66	138	12	112	16

* Received 2 cc. undiluted umbellulone intravenously.

TABLE V.—CHLORETONE ANÆSTHESIA COMPARISON ON DOGS.

Dog.	Age. Months.	Sex.	Weight, Kilos.	40% Chloretone. Cc.	Anæsthesia Time Minutes.
1	24	Male	17.0	20.4	8
2	12	Male	11.2	13.5	9
3	15	Female	11.2	13.5	8
4	10	Female	11.2	13.5	15
5	12	Male	11.3	13.8	8
6	9	Male	11.2	13.0	18
7	8	Male	9.7	11.0	20

NOTE: Time elapsing between injection of anæsthetic and operation was $2^1/_2$ hours in each case.

Post-mortem examination showed congestion of the lungs with blood clots. The heart stopped in diastole. The heart and the superior and inferior vena cava were dilated as were the other great vessels.

SUMMARY.

1. Umbellulone in blood produced methemoglobin *in vitro* and *in vivo*.
2. Umbellulone produced decided hemolysis of human, guinea-pig and horse blood.
3. Umbellulone injected intraperitoneally in guinea pig caused asphyxiation followed shortly by death.
4. Inhalation of umbellulone by guinea-pig irritated mucous membranes of eyes and nose caused irregular respiration at times but no failure of respiration.
5. Umbellulone in dilutions of 1:50 killed *Monilia tropicalis*, and *Trychophyton interdigetale* in 1-, 30- and 60-minute contacts. In dilutions of 1:100 the 1-minute contact was positive and the 30- and 60-minute contact negative.
6. Umbellulone in the presence of blood, peptone and gelatine showed but a slight loss in fungicidal power.
7. Umbellulone killed *E. typhi* and *Staph. albus* in dilutions as high as 1:500 for 15 minutes' contact. The estimated phenol coefficient was 6.25.
8. Umbellulone produced a decrease in frequency of the frog heart; loss of tonus and a decrease in the ventricle contraction. Stoppage of the heart occurred in diastole. Atropine, caffeine or adrenaline injected into the right atrium had no effect upon the paralyzed heart.
9. Results obtained on frog heart showed that umbellulone probably acts upon the same nerves and fibres as does atropine.
10. Umbellulone on isolated segment of rabbit and cat in 1:100,000 dilution produced slight stimulation; in dilutions of 1:40,000 or less, produced an apparent state of depression which progressed into partial paralysis. The length of time the paralysis was in effect depended on the degree of concentration of the solution; the more concentrated the solution the longer and the more complete the paralysis.
11. Intravenous injections of umbellulone caused a lowering of blood pressure and failure of respiration in dogs.
12. The clinical results and post-mortem examinations indicated that:

    a. Umbellulone probably acts as a depressant.
    b. Umbellulone produces rapid methemoglobin.

c. Umbellulone apparently caused pulmonary circulation to be blocked.

d. Umbellulone causes vaso-dilation of the heart and large vessels.

e. The minimal lethal dose of umbellulone in dogs is about 0.178 cc. per Kg. of body weight, death being due to failure of the respiration followed in a few minutes by stoppage of the heart.

REFERENCES.

(1) Jepson, W. L., "The Silva of California," 2, 243, University Press, Berkeley (1910).
(2) Douglass, D., "Douglass' Journal," 67 (1823–1827), W. Wesley and Son (1914).
(3) Benson, G. T., "Trees and Shrubs of Western Oregon," 2, 67, Stanford Publication (1930).
(4) Heaney, H., PROCEEDINGS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 23, 105 (1875).
(5) Stillman, J. M., *Amer. Chem. J.*, 2, 38 (1880).
(6) Powers, F. B., and Lee, F. H., *Jour. of Chem. Soc.*, 85, 629 (1904).
(7) Tutin, F., *Ibid.*, 89, 1104 (1906); *Ibid.*, 93, 252 (1908).
(8) Semmller, F. W., *Chem. Abs.*, 2, 837 (1908).
(9) Spiegel, L., "Chemical Constitution and Physiological Action of Drugs," 73–76, D. Van Nostrand Co. (1915).
(10) Parry, E. J., "Chemistry of Essential Oils," 237, Scott, Greenwood and Sons (1908).
(11) Sawyer, J. C., "Odorographia," "A Natural History of Raw Materials and Drugs Used in the Perfume Industry," 64, Gurney and Jackson (1894).
(12) Wienhaus, H., and Todenhofer, K., *Berichte der Schimmel and Co.*, 285, Jubileums-Ausgabe (1929).
(13) Kamm, O., "Qualitative Organic Analysis," Ed. 2, 129, John Wiley and Sons (1932).
(14) Russell, E. R., *Thesis*, Oregon State College. Unpublished (1929).
(15) Dessemontit, E., *J. Pharmacol. and Exper. Therap.*, 31, 377 (1927).
(16) Halliburton, W. D., "The Essentials of Chemical Physiology," Ed. 11, 249, Longmans, Green and Co. (1922).
(17) Pembrey, M. S., and Phillips, C. D. F., "The Physiological Action of Drugs," 5, Edward Arnold, London (1901).
(18) F. D. A., *U. S. D. A. Circular* No. 198, 11–12 (1931).
(19) Miller, Ruth, *Am. J. Pharm.*, 103, 324 (1931).
(20) Kingery and Adkison, *Arch. Dermat. and Syphilol.*, 17, 499 (1928).
(21) Salant, W., and Mitchell, C. W., *J. Physiol.*, 39, 355–374 (1916).
(22) Kamm, O., Aldrich, T. B., Grote, I. W., Rowe, L. W., and Bugbee, E. P., *J. Am. Chem. Soc.*, 50, 581 (1928).
(23) Jackson, D. E., "Experimental Pharmacology," 37, 85, Mosby and Co. (1917).
(24) Pittenger, P. S., "Biologic Assays," Ed. 2, 67–68, P. Blakiston and Sons, Inc. (1928).

FURTHER STUDIES ON PSYLLIUM SEED.*,[1]

BY HEBER W. YOUNGKEN.

In an article entitled "Studies on Commercial Psyllium Seeds" which appeared in Vol. XXI, No. 12, pages 1265–1273 of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, the writer discussed some earlier studies he had made on various commercial varieties of Psyllium. Since that time he has examined new lots of Psyllium seeds imported from Spain and France. He has also studied plants with mature fruit and seed bearing spikes from growers of commercial Psyllium seeds in France and Spain, and has compared these materials with authentic

* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] Massachusetts College of Pharmacy.

herbarium specimens in local herbaria and with standard descriptions of the species involved by Post (1), Reichenbach (6) and Hegi (2), thus enabling identification of the plants. Commercial seeds of *Plantago psyllium* L. and of *Plantago arenaria* Waldst. *et* Kit. [*P. ramosa* (Gilibert) Aschers] were planted in pots in a greenhouse and plants reared therefrom which compared favorably with descriptions of these species in the literature.

The seeds from a large number of recent commercial lots of Psyllium labeled French and Spanish Psyllium were also compared with seeds obtained from the fruits of the identified mature plants furnished by French and Spanish growers of Psyllium and the sources of four different kinds of seeds definitely established. It was found that most of the samples (in original packages with a Spanish label) labeled "Spanish Psyllium" were yielded by *Plantago psyllium* L., a few by *Plantago arenaria* Waldst. *et* Kit. and a number (with English labels) by *Plantago lanceolata* L., the last species being also the source of German Psyllium, also that most of the more recent "French Psyllium" samples were yielded by *Plantago arenaria*, a number by *Plantago psyllium* while occasional lots contained mixtures of *P. arenaria*, *P. psyllium* and *P. Cynops* or of *P. arenaria* and *P. Cynops*. It has also been ascertained that the seeds of *Plantago lanceolata L.*, previously described by the writer (4) are torrefied abroad and mixed with untorrefied seed of *Plantago arenaria* and offered in this combination to the American trade as French or Black Psyllium Seed.

Fig. 1.—*Plantago psyllium* L. Upper portion of leaf and flowering stem × 5/12.

Fig. 2.—*Plantago arenaria* W. *et* K. Terminal portions of leaf and flowering branches × 5/12.

A binocular dissection microscope was employed in the examination of the external morphology of the seeds. Cross sections were then made through the region of the cotyledons and raphe, mounted in glycerin and alcohol as well as in water and then studied under the compound microscope. The mucilage swelling factors were ascertained by the method outlined in a previous paper by the author (3).

From the studies made, the following descriptions are given for three authentic seeds of caulescent species of *Plantago* variously found in lots of French and Spanish Psyllium seeds.

PLANTAGO PSYLLIUM SEED.

The seeds examined were hemianatropous, silky to the touch, ovate to ovate elongate, larger at one extremity than the other, concavo-convex, light brown to chestnut brown, dark brown along the margin, very shining, mostly from 1.28 mm. to 2.72 mm. in length, rarely up to 3 mm., and from 0.6 to 1.12 mm. in breadth, the convex dorsal surface smooth, somewhat transparent and showing beneath the seed coat a light brown longitudinal area, representing the straight embryo, extending nearly the length of the seed, the hypocotyl being in the broader end and the cotyledons in the narrower end, the concave surface showing a large cavity, limited by the border which is raised as a cushion. The curved edge of the cushion forms a pointed, obtuse or right angle with the internal face of the cavity. In the center of the base of this cavity is an oval white scar representing the hilum. Occasionally, the raphe is present attached to one edge of the seed. A transverse fissure or groove is usually visible on the convex side and edges of most of the seeds. This is nearer the broader than the narrower extremity, and just over the point of union of hypocotyl and cotyledons. On the broader end of the seed may be seen the dark brown marks of the fusion of the seed coat at the end of the groove. The seeds are silky to the touch. 100 seeds weighed 0.072 Gm.

Fig. 3.—*Plantago Cynops* L. × 5/12.

Fig. 4.—Seeds of *Plantago psyllium* L. × 10.

Upon soaking the seed in water, the seed coat swelled and the seed became enveloped with a transparent, colorless mucilage. When the swelling phenomenon is observed under the microscope, it is noted that the epidermal cells elongate and their outer and radial walls become transformed to mucilage. The mucilage swelling factor in 24 hours varied from 12 to 16, and in 48 hours was up to 35.

Histology.—Transverse sections of *P. psyllium* seed cut through the central region possess a reniform outline and present for examination a spermoderm, endosperm and embryo. The spermoderm shows (1) an outer epidermis of mucilaginous epidermal cells with more or less obliterated walls in glycerin mounts, the radial and inner walls of which swell and disintegrate to form a clear mucilage upon irrigation of the mount with water, (2) a pigment layer with brown amorphous content. Directly beneath the spermoderm lies the broad endosperm, composed of irregular shaped, thick-walled cells with walls of reserve cellulose and intercellular-air-spaces. The outer layer of this region consists of palisade cells which range from 15μ to 34μ, rarely

to about 40μ in height. The contents of these endosperm cells consist of aleurone grains and fixed oil.

The straight embryo lies in the center of the endosperm and consists of 2 elongated, plano-convex cotyledons and a cylindrical hypocotyl. The cells of the embryo contain aleurone grains of varying shape up to 8μ in diameter and fixed oil. Three plerome bundles extend through the mesophyll of each of the cotyledons.

Fig. 5.—Seeds of *Plantago arenaria* W. *et* K. × 9.

PLANTAGO ARENARIA SEEDS.

The seeds observed differed from those of *P. psyllium* by the following characters:

They were darker brown to maroon in color, ovate-oblong to elliptical, less shiny, often dull, and rough and reticulate on the outer surface, with a median transverse groove or fissure or dent more distinct and usually nearer an equal distance from the two extremities than in *P. psyllium* and *P. Cynops* seeds. The ventral or concave surface shows averagely a broader cavity than in *P. psyllium* seed and the edge forms a somewhat flattened cushion instead of a rounded one. Moreover, as François (5) has shown, this edge forms a sharp indented angle with the base of the cavity. The size of *P. arenaria* seeds ranged from 1.6 mm. to 3 mm. in length and from 0.96 mm. to 1.5 mm. in breadth. The hilum at the bottom of the cavity was pale brown to occasionally whitish. 100 seeds weighed 0.0842 Gm. Their mucilage swelling factor in 24 hours was averagely 8, whereas that of *P. psyllium* seed was averagely 14 and varied from 12 to 16. The palisade cells of the endosperm were from 15μ up to about 52.5μ in height.

PLANTAGO CYNOPS SEEDS.

This seed is larger than those of the other two species, ranging from 3 to 4 mm. in length and up to 2 mm. in breadth. It is ovate-oblong, enlarged at one extremity and strongly contracted at the other, dull brown to dull greenish brown, with a transverse depression nearer the broader than the narrower end. It is convex on the dorsal surface with a broad, deep concavity on the ventral surface which is open at the contracted end. The edges are curved into the cavity. A whitish hilum is found at the base of the ventral cavity. 100 seeds weighed 0.1649 Gm. The palisade cells of its endosperm were from 15μ to 48.75μ in length.

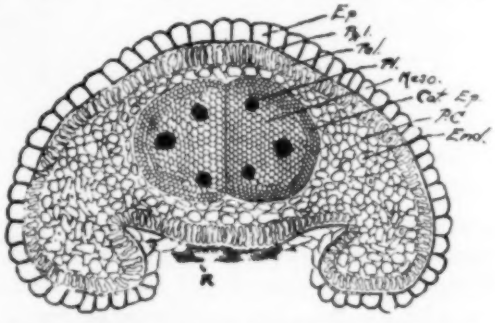


Fig. 6.—Transverse section of *Plantago arenaria* seed × 40.

Ep, epidermis and Pgl, pigment layer of seed coat; Pal, palisade layer of endosperm; End, inner region of endosperm which contains fixed oil and aleurone but no starch; PC, protoplasmic connections between inner endosperm cells; Cot. Ep., epidermis of cotyledon; Meso, mesophyll of cotyledon; Pl, plerome bundle; R, raphe.

The mucilage swelling factor of one lot taken after 24 hours was 1 and after 48 hours 1.5. The writer anticipates additional work on the mucilage swelling factor of this seed as more material becomes accessible.

CONCLUSIONS.

1. It is ascertained that good French and Spanish Psyllium Seeds of the current American market are yielded by *Plantago psyllium* and *Plantago arenaria*.

2. *Plantago psyllium* seed is superior to *Plantago arenaria* seed in mucilage swelling capacity.

3. Most of the French Psyllium seed is now yielded by *Plantago arenaria*, less by *P. psyllium* while occasional lots contain mixtures of *P. arenaria*, *P. psyllium* and, rarely, *P. Cynops*.

Fig. 7.—Seeds of *Plantago Cynops* L. × 6.5.

REFERENCES.

(1) Post, G. E., "Flora of Syria, Palestine and Sinai," pages 671–672 (1896).

(2) Hegi, Gustav, "Illustr. Flora von Mittel Europa," Bd. vi, page 193.

(3) Youngken, H. W., JOUR. A. PH. A., 21, 1272 (1932).

(4) *Ibid.*, pages 1269–1271.

(5) François, L., "Différents Types de Graines du Genre Plantago," Dunod, Paris, 7–9 (1933).

(6) Reichenbach, H. G. L., "Incones Floræ Germanicæ et Helveticæ," 17, Pl. 1135, 1136 (1855).

CRYSTALLINE FORMS OF EPHEDRINE ALKALOID.*

BY E. E. MOORE AND D. L. TABERN.

Ephedrine alkaloid as it appears on the market was found to exist in two forms, one containing about 95 per cent of the alkaloid, and five per cent of water, while the other assays nearly 100 per cent. Although the former is crystalline, while the latter is usually an oil or a rock-like solid, assays of the latter indicated that the more nearly the composition approached the anhydrous, the higher the melting point.

Emde (1) reported an ephedrine hydrate containing about 10 per cent of water which would correspond to one mol. of water for each mol. of ephedrine. However, samples of hydrated ephedrine obtained from different manufacturers, or prepared by recrystallizing the alkaloid from water, were assayed in this laboratory and found always to contain about 5 per cent of water. This would correspond to a hemi-hydrate, rather than a hydrate.

The purpose of this work was to prove that the hemi-hydrate is the usual hydrate of ephedrine, to determine the melting point of anhydrous ephedrine, and to ascertain the effects of different amounts of water on this melting point.

* Abbott Laboratories, North Chicago, Ill.

Received October 17, 1934.

METHOD.

Ephedrine alkaloid N. N. R. was distilled at 25 mm. Any water which was present came over quickly. When the temperature reached 150°, the receiver was changed and distillation continued. The anhydrous base boiled over within the range, 151–153°. A number of different distillates solidified within the range, 38.0–38.1°.

Fifteen to 30 Gm. of the molten anhydrous alkaloid obtained above accurately weighed was placed in a small round-bottom flask, fitted with a stopper having holes for an Anschutz thermometer and a stirring rod. The apparatus was cooled to 30° C. and the ephedrine seeded with a small crystal of anhydrous base. The mass was stirred and the temperature rose to a constant value—the solidification temperature—where it remained for some time.

The mass was melted, a known weight of water added and incorporated thoroughly with the ephedrine. The solidification temperature was determined by the same procedure used for the anhydrous base.

The above was repeated, adding successive small quantities of water, until the desired number of values was obtained.

Three such experiments were carried out, using different samples of anhydrous base and the points obtained were found to fall on the same curve. (Table I), (Curve I), Fig. 1.

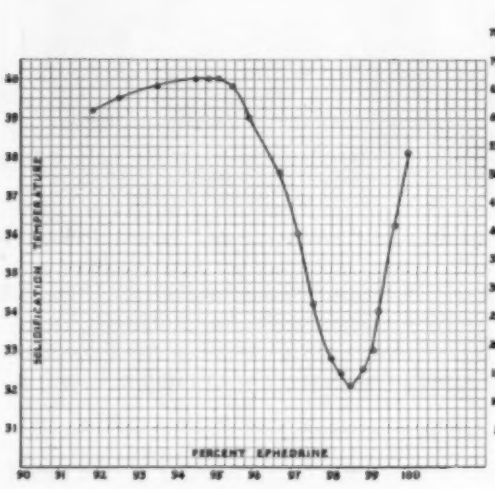


Fig. 1.—Solidification temperature.

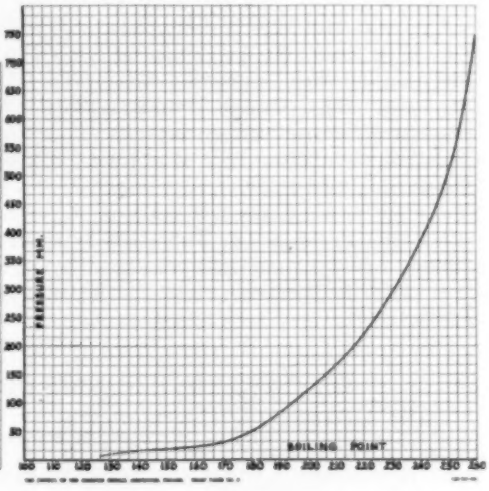


Fig. 2.

The values for the anhydrous base and for the base with a half mol. of water were checked by melting point determinations.

The solidification temperature can be determined with as little as 2 Gm. of ephedrine, if a small insulated test-tube is employed as the container. This modified technique has been found to be very useful as a rapid method of determining the purity of the alkaloid.

Anhydrous ephedrine melts at 38.1°. The addition of water lowers the melting point until with 1.5 per cent a eutectic mixture, ephedrine-ephedrine hydrate melting at 32.1° is obtained. Further addition of water raises the melting point until with five per cent a maximum of 40° occurs. The composition of this last substance corresponds closely to that of a hemi-hydrate.

Incidental to the purification of anhydrous ephedrine base by distillation, the boiling point was determined at various pressures in the range of 65 and 760 mm. (Table II), (Curve 2), Fig. 2. This supplements the data between 7 and 25 mm. reported in the A. D. M. A. proceedings for 1933. (2) Above 250° slow decomposition seemed to ensue.

TABLE I.—SOLIDIFICATION TEMPERATURES. SYSTEM, EPHEDRINE–WATER.

Per Cent.			Per Cent.		
Ephedrine.	Water.	Solidification Temperature.	Ephedrine.	Water.	Solidification Temperature.
100.00	0.00	38.1	97.15	2.85	36.0
99.65	0.35	36.2	96.65	3.35	37.6
99.25	0.75	34.0	95.85	4.15	39.1
99.10	0.90	33.0	95.45	4.55	39.8
98.80	1.20	32.5	95.10	4.90	40.0
98.50	1.50	32.1	94.85	5.15	40.0
98.45	1.55	32.1	94.50	5.50	40.0
98.25	1.75	32.4	93.50	6.50	39.8
98.00	2.00	32.8	92.50	7.50	39.5
97.55	2.45	34.2	91.85	8.15	39.2

TABLE II.

Press. Mm.	B. Pt.	Press. Mm.	B. Pt.
745	260	65	185
645	257	32	172
545	253	A. D. M. A. Proc. 1933 (2)	
445	246	25	152–153
345	237	20	146–148
245	224	10	132–133
145	205	7	127–128

When the distilled anhydrous base was crystallized from an anhydrous medium, such as dry ether, crystals were obtained which analyzed 100 per cent ephedrine. When crystallized from water or dilute alcohol, the crystals analyzed 95 per cent.

The anhydrous crystals were very hygroscopic, while the hydrated material did not tend to take up or give off water.

Dr. George L. Clark has kindly studied the crystalline forms of the anhydrous and hydrated bases and found them to be different.

SUMMARY.

Crystalline anhydrous ephedrine was prepared and its melting point determined.

The existence of a hemi-hydrate of ephedrine containing 95 per cent of the base was proved. The anhydrous and hydrated alkaloids differ in crystalline form, melting point, stability and solubility in oil.

The effects of different amounts of water on the melting point of ephedrine were determined.

REFERENCES.

(1) Emde, H., *Helv. Chim. Acta*, 12, 365 (1929).
(2) Am. Drug. Mfrs. Assoc., *Proc.*, 235 (1933).

DISPENSARY SERVICE.

Dispensary service owes its existence to the great London fire in 1666. The Pennsylvania Hospital established the first dispensary in this country (1751).

PHYTOCHEMICAL NOTES.

FROM THE LABORATORY OF EDWARD KREMERS.

No. 111. The Sterols from Monarda Fistulosa.

BY OLE GISVOLD.

The unsaponifiable material prepared by E. J. Ireland from the saponified fatty oil obtained from the leaves of the wild bergamot was imperfectly crystalline. The several fractions submitted were combined, dissolved in ether, alcohol added to the ethereal solution, also some charcoal. The mixture was heated to boiling for a few moments and then filtered. After filtration, the ether was evaporated off and water added to the hot solution until the precipitate produced just redissolved.

Upon recrystallization beautiful leaflets were thus obtained. They melted at 130–131° and showed no change in melting point after drying at 100° also over P_2O_5 in a vacuum.

The sterol was acetylated. The acetylated product, upon crystallization, melted at 115°. Upon recrystallization the product softened at 115° and became clear at 118°.

The absence of stigmasterol was indicated when tested for by the method of Windaus and Hauth.[1] However, reinvestigation of larger amounts, when available, may yet prove the presence of stigmasterol with a sitosterol.

The Therapy of the Cook County Hospital. Edited by Bernard Fantus, M.D., Chicago.—In their elaboration, these articles are submitted to the members of the attending staff of the Cook County Hospital by the director of therapeutics, Dr. Bernard Fantus. The views expressed by various members are incorporated in the final draft for publication. The series of articles will be continued from time to time in the columns of the *Journal A. M. A.*

The following prescriptions were selected from one of a series of articles in the *Journal A. M. A.* by the *Prescriber* and edited by this publication in accordance with the British Pharmacopœia.

Rubefacient Pigment.

℞ Menthol..... 2.0 Gm.
Volatile Oil of Mustard... 2.0 ml.
Alcohol (95 per cent)..... 50.0 ml.

Mix. Apply a few drops to the affected area. (Avoid the vicinity of the eyes.)

Analgesic Pigment.

℞ Camphor
Chloral Hydrate
Menthol, of each..... 30.0 Gm.
Alcohol (95 per cent), to make..... 120.0 ml.

Mix. Paint over painful area.

Combined Analgesics.

Dry Extract of Hyoscyamus..... 0.15 Gm.
Acetanilid..... 1.00 Gm.
Acetylsalicylic Acid..... 5.00 Gm.

Mix and divide into 15 capsules. One every two to four hours as required. (The analgesic effects of acetanilid and acetylsalicylic acid are enhanced by this combination and the sudorific effect is arranged by the hyoscyamus.)

Benzocaine-Camphor Oil.

℞ Benzocaine..... 2.0 Gm.
Liniment of Camphor to.. 100.0 ml.

Mix. Apply freely on gauze as a dressing for painful wounds of ulcers.

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[1] *Ber.*, 39, 4381 (1906).

EMINENT AMERICAN PHARMACOGNOSISTS OF THE NINETEENTH CENTURY.

BY HEBER W. YOUNGKEN.

(*Concluded from page 152, February Journal.*)

ALBERT SCHNEIDER (1863–1928).

Albert Schneider was born in Granville, Illinois, April 13, 1863. His boyhood days were spent on his parent's farm in McLean County, Illinois, where he worked during the summer and attended the district schools for a few months each winter. At the age of seventeen he entered Valparaiso, Indiana Normal School, where he intended to prepare for medicine but was compelled to relinquish his studies after about six months on account of an attack of inflammatory rheumatism. After recovering he entered the Dixon, Illinois Normal School and completed his preparatory studies. He then went to Chicago for the study of medicine. He was graduated from the College of Physicians and Surgeons of Chicago in 1887, the same year he received his Bachelor of Science degree from the University of Illinois. He took graduate work at the University of Minnesota and obtained his M.Sc. from that institution in 1894, and his Ph.D. from Columbia University in 1897. He held the Fellowship in Botany at Columbia for two years, making a special study of Lichens. During a portion of his stay at the University of Minnesota he served as Instructor in Botany in that institution.

ALBERT SCHNEIDER.

After graduation from Columbia he was called to the chair of Pharmacognosy and Bacteriology in the Northwestern University School of Pharmacy where he remained until 1903. From 1903–1919 he served as professor of Pharmacognosy and Bacteriology, and from 1904–1906 as professor of Materia Medica and Therapeutics in the University of California. While there he also filled outside positions. From 1906–1907 he was director of the Spreckel's Sugar Company Experiment Station, and from 1909–1915 pharmacognosist for the U. S. Dept. of Agriculture; from 1915–1919, microanalyst of the California State Food and Drug Laboratory, and from 1910–1915 was editor-in-chief of the *Pacific Pharmacist.* In 1919, he resigned his position at the University of California to accept the chair in Pharmacognosy at the University of Nebraska which he held until 1922 when he was called to the position of dean of the School of Pharmacy of North Pacific College, Portland, Oregon. He served for many years as a member of the Revision Committee of the United States Pharmacopœia on which he helped draft the monographs on powdered vegetable drugs. He was president of the American Conference of

Pharmaceutical Faculties from 1913–1914, and lecturer for several years in the Portland Police School and summer school of the University of California on crime investigations.

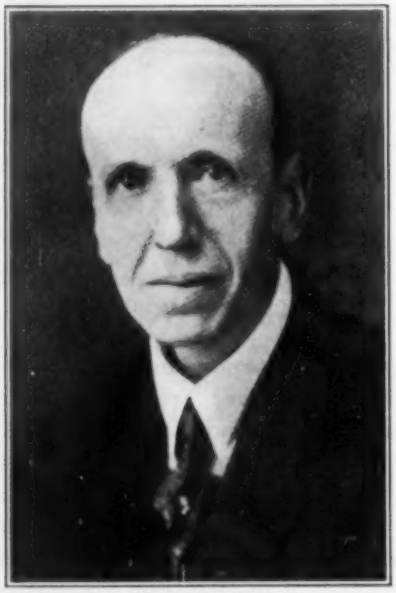
Professor Schneider's activities covered a wide field; he possessed a profundity of thought and a versatility of knowledge. He was always outspoken with his opinions. He was a frequent contributor of scientific articles upon microscopical subjects in which he was an investigator of marked ability. He also wrote on Coto, Paracoto, Winter's Bark and many other themes. His outstanding works were as follows: "Primary Microscopy and Biology," 1890; "Text-Book on General Lichenology," 1897; "Guide to the Study of Lichens," 1898; "Microscopy and Micro-Technique," 1899; "Hints on Drawings for Students of Biology," 1899; "General Vegetable Pharmacography," 1900; "Powdered Vegetable Drugs," 1902; "Bird and Nature Study Chart Manual," 1903; "Medicinal Plants of California," 1909; "Pharmaceutical Bacteriology," 1920; "The Microbiology and Analysis of Foods," 1920; and a "Translation of Westermaier's Compendium der Allgemeinen Botanik," 1896.

Dr. Schneider became internationally known for his work in the later years of his life on crime detection. He was an inventor of a lie detector, and also of a ventilating system for Pullman cars.

He died suddenly as a result of a cerebral hemorrhage on October 27, 1928, while on his way to the college.

HENRY KRAEMER (1868–1924).

Henry Kraemer was born in Philadelphia, Pa., July 22, 1868. He received his early education in Girard College from which he graduated in 1883. He then entered the drug store of Dr. Clement B. Lowe where he served an apprenticeship of five years, attending the Philadelphia College of Pharmacy during part of this apprenticeship from which institution he was graduated in 1889 with honors. During his senior college year and the following year he served as assistant in general chemistry to Professor Sadtler at the University of Pennsylvania.



HENRY KRAEMER.

In 1890 he became Instructor in Botany and Pharmacognosy in the College of Pharmacy of the City of New York. Desiring further training in the natural sciences, he took a special course in botany at Barnard College and in 1891 entered the School of Mines of Columbia University from which he graduated with a Ph.B. in 1895. While a senior at Columbia he was elected Professor of Botany, Pharmacognosy and Materia Medica in the School of Pharmacy of Northwestern University with one year's leave of absence before entering on his duties. He spent this year abroad at the

University of Marburg (Germany) studying under Meyer, Cohen, Zincke and Melde, and received the degree of Ph.D. cum laude in June 1896. His doctorate thesis was on "Viola tricolor." He then assumed his duties at Northwestern University but resigned at the end of the year to accept the chair in Botany and Pharmacognosy at the Philadelphia College of Pharmacy in the Fall of 1897.

In 1899 he became editor of the *American Journal of Pharmacy*, succeeding Professor Henry Trimble, and he made a large number of contributions to this *Journal* during his nineteen years of editorship.

While at the Philadelphia College of Pharmacy he became a voluminous contributor to the literature of botany and pharmacognosy. He wrote textbooks on botany and pharmacognosy, applied and economic botany, and scientific and applied pharmacognosy; he also published many papers on a variety of topics pertaining to pharmacognosy, the outstanding of which are as follows: "Calcium Oxalate Crystals in the Study of Vegetable Drugs;" "Effect of Heat and Chemicals on the Starch Grain;" "Some New Methods in the Study of the Commercial Starches;" "Valuation of Vegetable Drugs and Foods;" "Microscopical and Chemical Examination of Cloves;" "Assay of Drugs by the Use of Living Plants;" "The Nature and Structure of Cochineal;" "Substitution of the Fruits of Rhus Typhina for Rhus Glabra;" Histology of the Rhizome and Roots of Phlox Ovata;" "Adulteration of Marjoram and Coriaria;" "Some of the Distinguishing Morphological Characters of Belladonna and Scopola;" "Plant Colors;" and "Color Standards of Powdered Vegetable Drugs."

In addition to his regular courses, he introduced and carried on special courses at the college on the microscopical examination of foods and technical products and in bacteriology. He was always popular with his students, many of whom sought his counsel.

In 1900 he became a member of the Committee of Revision of the United States Pharmacopœia and was made chairman of the Sub-Committee on Botany and Pharmacognosy which position he held through the revision period of 1910 and a portion of the period of 1920. He was president (in 1917) of the American Conference of Pharmaceutical Faculties and the Philadelphia Botanical Club.

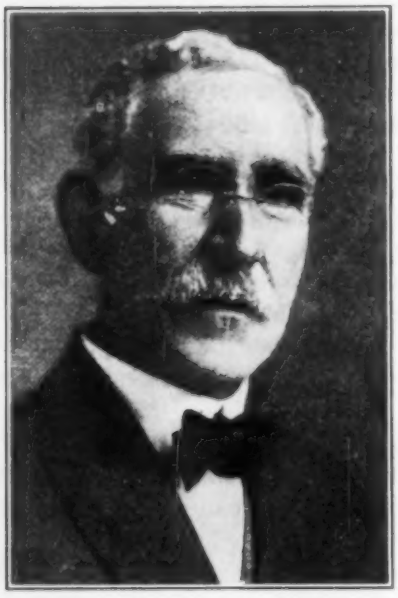
In 1917 he resigned his position at the Philadelphia College of Pharmacy to become Dean and Professor of Pharmacognosy at the University of Michigan. In 1920 he resigned from this position and moved to Mount Clemens, Michigan, where he opened an office and laboratory as a consulting bacteriologist and chemist. He died at Mount Clemens, September 9, 1924.

LUCIUS E. SAYRE (1846–1924).

Lucius Elmer Sayre was born in Bridgeton, New Jersey, November 2, 1846, where he received his early education in the public schools and as an apprentice in the drug store of Robeson and Whitaker. In the early sixties he came to Philadelphia and clerked in the drug store of Dr. L. Updycke while attending the Philadelphia College of Pharmacy from which he graduated in 1866. He then obtained a position in the pharmaceutical laboratory of Frederick Brown and, later, with Henry C. Blair's Sons, Apothecaries, in Philadelphia.

Sayre was a close friend and classmate of Professor Remington and in 1879 they opened a drug store as partners at 18th and Market Streets, Philadelphia, in which they manufactured a number of pharmaceuticals including scale pepsin. During the partnership, Sayre became a quiz master in materia medica of the Alumni Association of the Philadelphia College of Pharmacy and lecturer on pharmacy in the Women's Medical College of Philadelphia.

Upon the founding of the School of Pharmacy at the University of Kansas in 1885, Mr. Sayre was elected dean and also professor of Materia Medica and Pharmacy. In 1907, Professor Sayre became director of drug analysis for the Kansas State Board of Health and a member of the botanical staff of the Kansas State Board of Agriculture.



LUCIUS E. SAYRE.

He received an honorary Bachelor of Science degree from the University of Michigan in 1896 and the Master of Pharmacy degree from the Philadelphia College of Pharmacy in 1897. He was a member of the Revision Committees of the United States Pharmacopœia of 1890, 1900 and 1910, chairman of the Scientific Section in 1893 and of the Historical Section of the A. PH. A. in 1917, and president of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1919–1920.

Professor Sayre contributed a variety of papers embracing historical, botanical, pharmacognostical and chemical subjects. He was especially interested in the proximate analysis of vegetable drugs and foods. He wrote several papers on the alkaloids of Gelsemium and others on the analysis of Gymnocladus Seed, "Assay of Datura Stramonium," "Cactus Grandiflorus," "Drug-Eating Insects," "Drug Culture," "Euphrasia," "Oregon Balsam," "Golden Seal Gardens," "Characters of Distinction of Viburnum Prunifolium and Viburnum Opulus," and "Viburnum Barks, Microscopical Distinctions." He collaborated with D. H. Robinson, professor of Latin at the University of Kansas, on Robinson's Latin Grammar of Pharmacy and Medicine. His best known work was "Organic Materia Medica and Pharmacognosy" which extended through four editions.

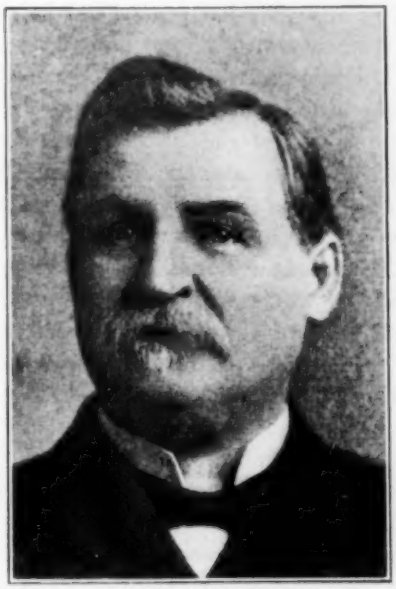
He died at Lawrence, Kansas, on July 21, 1924. Professor Sayre was a leader in the development of the teaching of materia medica and pharmacognosy, a modest yet impressive worker, and a great figure in American Pharmacy.

OTTO A. WALL (1848–1922).

Otto Augustus Wall was born in St. Louis County, Missouri, on September 27, 1848, the son of a German clergyman. He received his early education in the schools of St. Louis and in 1864 entered the drug store of Dr. Sanders. During his apprenticeship under Dr. Sanders he attended the St. Louis College of Phar-

macy from which institution he graduated in 1868. He then entered the Missouri Medical College, receiving his M.D. in 1870. He also graduated from the Bellevue Hospital Medical College, New York, in 1871. From 1869–1873 he was proprietor of a drug store in St. Louis.

Upon returning to St. Louis he became professor of Materia Medica, Pharmacognosy and Botany in the College of Pharmacy, a position which he held for forty-nine years. He was also professor of Therapeutics and Materia Medica in the Missouri Medical College.



OTTO A. WALL.

In 1882 he and Dr. Oldberg established the Oldberg-Wall Laboratory. At one time he was a member of the editorial staff of the *National Druggist* and editor of the college publication. He was a member of the U. S. P. convention from 1880–1920 and a member of the U. S. P. Revision Committee 1880–1900, and presided over the U. S. P. convention of 1910. He was also president of the Missouri Pharmaceutical Association from 1883–1885.

Dr. Wall was a large man with an impressive bearing. He was affable and warm hearted, very apt with the pen and brush and an excellent parlimentarian. His brain was a vast storehouse of facts covering a wide field of general knowledge and he was a very popular teacher. He was noted for the study of sections of drugs with the microscope and for making lantern slides of these.

His best known contributions in pharmacognosy are his "Notes on Pharmacognosy," and "Handbook of Pharmacognosy," the fifth edition of which was revised in 1928 by Professor Leo Suppan. Wall was also author of "The Prescription," "Latin for Pharmacy and Medical Students," "Sex Worship," etc. He was co-author with Dr. Oldberg of "The Companion to the Pharmacopœia." He also wrote a number of papers, the last of which entitled "Vegetable Taxonomy" was presented at the 1916 meeting of the A. PH. A.

Professor Wall died of heart failure on February 13, 1922, in his 76th year.

MEETING OF THE NATIONAL ACADEMY OF SCIENCES AND OF THE EXECUTIVE COMMITTEE OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

The annual stated meeting of the National Academy of Sciences will be held under the presidency of Dr. W. W. Campbell, in the building of the academy at Washington, on April 22nd, 23rd and 24th. The autumn meeting will be held at the University of Virginia on November 18th, 19th and 20th.

The spring meeting of the Executive Committee of the American Association for the Advancement of Science will be held in New York City on April 14th. Communications to be brought to the attention of the committee should be sent to the permanent secretary, the Smithsonian Institution Building, Washington, D. C.

HISTORY OF HAMAMELIS (WITCH HAZEL),*[1] EXTRACT AND DISTILLATE.

BY JOHN URI LLOYD AND JOHN THOMAS LLOYD.[2]

In 1865, the senior member of the writers of this treatise was acting as clerk in the establishment of W. J. M. Gordon and Brother, Ninth and Central Avenues, Cincinnati, Ohio.

Mr. Gordon specialized in physicians' supplies, and made a feature of the "Concentrations" and other Eclectic preparations, then rapidly coming into favor. This was natural, as the Gordon establishment was but two blocks from the Eclectic Medical Institute, Court and Plum Streets. Drs. King and Scudder, and other professors of the Institute, were patrons of the Gordon establishment, and contributed, constantly and helpfully, to Mr. Gordon's pharmaceutical researches. They naturally fraternized with the physicians of other schools, who met in Gordon's large, comfortable and hospitable front room, where all, alike, considered themselves at home. A "No Man's Land" it was, but one of cheer and helpfulness, not of war, personalities and misrepresentation. The physicians who there met, differed in views, but they personally respected each other's ideals and processes. They had no desire to suppress the efforts of others who were endeavoring to serve the needs of the American people. That was left to medical politicians.

At that time, 1865, Mr. Gordon had in his employ a business representative named Leon Hurtt, a brother of F. W. Hurtt, a banker in New York City. Through Leon, F. W. Hurtt proposed to purchase the right to make the preparation then known as "Pond's Extract." The senior writer of this chronicle well remembers when, in his presence, Leon Hurtt informed Mr. Gordon (who, I was told, had declined to purchase the Pond Extract rights) that he wished to resign his position with the Gordons, to devote his time to the introduction and sale of the proprietary medicine, "Pond's Extract;" it was then used almost exclusively by the Homeopathic medical profession of America, being scarcely known either to other physicians, or to the public generally.

In one of my visits (J. U. L.) to Los Angeles, California, I learned that Leon T. Hurtt was yet living, a resident of that city. I located his home, and in 1915 made him a personal visit, with the object of obtaining from him an authoritative statement concerning the history of Pond's Extract, as well as his connection therewith. In this and other later visits, he gave me in detail the history of the preparation, which was first a water-made extract, but is not now an "extract," although established and sometimes sold under that title. I have not hesitated to utilize Mr. Hurtt's words verbatim, as a part of this paper.

To the foregoing I will add that in my opinion the story herein told could not, at the date of my interview with Mr. Hurtt, have been handled authoritatively by

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* Section on Historical Pharmacy, Toronto meeting, 1932.

[1] Especially as related to the distillate, known first under the name "Golden Treasure," then as "Pond's Extract," and next as "Aqua Hamamelidis" (U. S. P. IX) and "Fluid Extract of Hamamelis" (N. F. V).

[2] The illustrations presented in this treatise, unless otherwise credited, are by John Thomas Lloyd. The Hamamelis shrub was photographed by him in the New York location where the Oneida Indians lived, and the experimental supplies mentioned in this article were obtained by him from the Oneida section.

any other person, he being the only living "charter member" of the organization originally known as the "Pond's Extract Company."

Pond's distilled hamamelis was quietly introduced into the Homeopathic school of medicine. Coming gradually into the practice of Eclectic physicians, creeping into that of Allopathic physicians, it finally came into the use of the public generally. The chemist, finding little in the distillate other than alcohol and traces of an essential oil, accepted that distilled hamamelis must, if it had any virtues, depend on the water and the alcohol it contained.

And yet, after many decades have passed, distilled hamamelis stands firmly entrenched as one of the most popular of physicians' favorites, being also largely employed as a toilet application in America. And that, too, in the face of resistance by authority such as Dr. John Marshall, and H. C. Wood, of Philadelphia who, in 1886, made a strenuous scientific laboratory investigation of hamamelis, deciding that there was nothing of therapeutic value in the distillate. Their article ended as follows:

"This much used, and still more lauded witch-hazel, or the so-called distillate of witch-hazel, must depend for its virtues upon the alcohol they contain, and the faith they inspire." This view is upheld by the *United States* and the *National Dispensatories*, as follows:

> "As whatever slight therapeutic virtues witch-hazel possesses seems to depend on its tannin, it is obvious that this distillate cannot represent the drug." *U. S. Dispensatory*.
>
> "The good that it exerts in the treatment of sprains, bruises, wounds, chilblains, sore eyes, headache, and a host of other conditions, resides more in the activity of a cleansing and evaporating lotion and in the mind of its user, than in any decided curative properties that the preparation may possess." *National Dispensatory*, 1916.

In this connection, I am of the opinion that no claim is made by any maker of the distillate that it represents the fixed astringent principles of the drug. Nor am I convinced that alcohol is the only serviceable content of the distillate.

"Golden Treasure"

As written by Leon T. Hurtt, of the Pond's Extract Company.

(Edited slightly in phrase directions L.)

"In the early 1840's, Theron T. Pond, a resident of Utica, New York, became interested in, and associated more—or less, with a tribe of Indians known as the Oneida tribe then located in Central New York. He found that they were using for burns, boils and wounds of every description a 'tea' made by their Medicine Man from a species of bush known as 'witch hazel,' a shrub supposed by them to grow only in Central New York. The Medicine Man made his extract by steeping the shrub in an ordinary teakettle. The liquid which he obtained was colored but as clear as water, and had a peculiar aroma obtained from no other shrub.

"The 'Witch Hazel' is peculiar (Cuts B & C), in that it blossoms in the fall, producing small, yellow flowers. The medicinal properties of the extract were, in the opinion of the Oneidas, remarkable. A sudden electrical and thunder storm (it was stated) would turn the liquid milky, but within forty-eight to seventy hours it would return to its original clearness.[1]

"Mr. Pond, believing in the wonderful medicinal properties of the 'Witch Hazel' tea, decided to learn from the Indian doctor the peculiar species of shrub used. With the Indian Medi-

[1] This needs corroboration. J. U. L.

cine Man he spent several months, searching the underbrush until he fully informed himself of the shrub they employed. He then formed with the Indians a sort of partnership to make the extract, putting it up in a shape to be sold among their friends.

Fig. A.—Indian medicine man.

"The Medicine Man was extremely particular about the species of shrub used, and its manipulation. He would gather it himself in the woods, bringing it in by the armful, and steeping it at once.

"At first they boiled the shrub in an ordinary iron kettle or cauldron, over a direct fire. Thus they produced a fair article, but they could not preserve it. After studying different preservatives, they finally used about 3% alcohol, but in warm weather that amount of alcohol failed to keep the product, and the alcohol was increased.

"They decided to give to their extract the trade name, *'Golden Treasure,'* a name suggested by Mr. Pond. After his death, this name was changed to 'Pond's Extract.'

"Mr. Pond and the Medicine Man worked together for several years, introducing the product mainly among their personal friends. They finally decided to put the 'Extract' on the market, and did so, in a local way, in 1848. When we sold the Pond's Extract Company, in 1898, there was in the company's safe a two-ounce bottle, made in 1848, which was apparently still good. Whether that bottle can now be found, I do not know.

"Theron T. Pond died some time between 1847 and 1850. It is said that he lost his life from exposure in the woods.

"Between 1846 and 1850, Pond and the Indian Medicine Man sold their business to Hart and Munson, iron foundry men of Utica, New York. They took in with them Isaiah A. Palmer, a friend and neighbor of Theron T. Pond. The business was next sold to a firm in New York whose name I have forgotten, but as no business of any consequence resulted, the company was sold by the sheriff. It was bought in by Isaiah A. Palmer, who claimed never to have sold his interest therein. It should here be repeated that Palmer, Hart and Munson had given the product the name 'Pond's Extract,' dropping the name 'Golden Treasure.'"

"Dr. Frederick Humphrey, a Methodist minister, and also a Homeopathic physician, proprietor of the Homeopathic Medicine Company, 562 Broadway, New York, claimed that for years he had been Mr. Pond's family physician, and that Pond had given him the right to manufacture and sell the extract through his 'Humphrey Homeopathic Medicine Company.' He did, indeed, commence to manufacture the same, continuing the name, 'Pond's Extract.' His claim was denied by Palmer, who commenced suit and applied for an injunction forbidding Humphrey from either using the name 'Pond's Extract,' or manufacturing the article.

"A party from Connecticut who had worked for the original firm of Pond and the Indian, also claimed that he had the right to make 'Golden Treasure,' but he was unable to establish his claim.

"At that time, the 'extract' was still made by using the old cauldron, over a direct fire. Palmer employed a copper kettle, with a very crude concentrating hood and worm. Cold water was used for condensing the vapor.

"In 1871 or '72, while the lawsuit (Palmer *vs.* Humphrey) was still pending, Mr. F. W. Hurtt, a banker of New York, bought the interest, or the alleged interest, of the Humphrey Homeopathic Medicine Company, and to quiet Palmer, took him into partnership, giving him an eighth interest in the new corporation, which was capitalized at $100,000.00. At that time, the sale of Pond's Extract was less than $5000.00 per annum.

"Harry Cole, of Cincinnati, myself and F. W. Hurtt, of New York, bought the concern, which we reorganized, electing F. W. Hurtt, *President*, L. H. Hurtt, *Vice-President*, Harry Cole,

Treasurer, and I. A. Palmer, *Manufacturer*. We transferred the company from 562 Broadway, New York, to 76 Williams Street, New York, the firm name now being, F. W. Hurtt and Brother, Wholesale Druggists. The company then had three factories, small and crude, with four kettles at each factory. One of these factories (all in New York State), was located at Tightsville, one at Little Falls, and one at Frankfort. These three factories I consolidated into one, at Rome, New York, and for four years ran that factory from November, each year, until April or May.

"In the meantime Isaiah A. Palmer had died, and E. D. Palmer, the sculptor, became interested with us. However, besides holding the office of vice-president and running the drug department after I. A. Palmer's death, I added to my other duties the manufacturing of the Extract.

"We then moved from Rome, New York, to Chester, Connecticut, the only other locality I knew where the Indian species of Witch Hazel was obtainable.[1] I immediately decided to build steam stills,[2] believing that I could obtain better extract from the shrub than I could with the old-time, direct fire, copper kettles. This I proved by making an extract nineteen per cent stronger than we had before obtained.

"About a year after our purchase of their alleged interest from Dr. Humphrey and the Homeopathic Company, Humphrey's Medicine Company sued us for reformation of contract and

Fig. B.—Witch-hazel flowers.

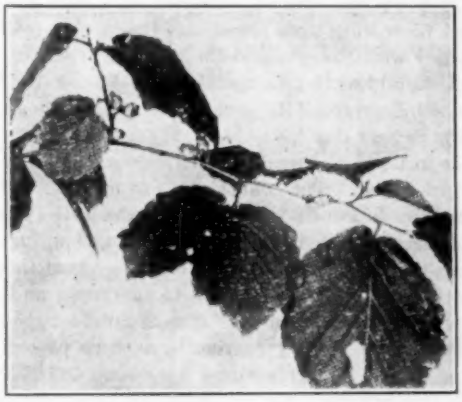

Fig. C.—Witch-hazel twig showing leaves and fruit.

agreement. We in turn enjoined them from using the term 'Pond's Extract,' or from manufacturing that product. This lawsuit was in the court for several years.

"The day after our charter was issued by the Secretary of State, our president, F. W. Hurtt, started on a trip around the world. It then became my duty to assume the entire responsibility of the company. We ran the Extract in connection with our wholesale drug business (F. W. Hurtt & Brother), but the establishment was inadequate for both the drug and medicine, and the Pond's Extract business. We therefore leased a whole building at 98 Maiden Lane, and there we conducted the business for five years, until 1878. On our president's return, and on account of the rapid increase of business, we bought a brick factory in Brooklyn, E. D., a four-story building one hundred feet square. This was used only for bottling and shipping, and for the Business and Advertising Departments of the Pond's Extract Company. Our distilleries were still in Chester, Connecticut.

"When the bridge crossing East River was built, the site of our building in Brooklyn was needed, and F. W. Hurtt bought the old Belmont home, 76 Fifth Avenue, New York, and No. 1, West 13th Street. This we remodeled, moving into it in 1883. As stated, we were then manu-

[1] For years I made distilled hamamelis from a grove of witch-hazel shrubs on the Licking River, Kentucky. J. U. L.

[2] The original "extract" abandoned. J. U. L.

facturing our Extract at Chester, Connecticut. There we abandoned the old kettle previously employed, changing to 400-gallon copper stills made under my own supervision. I understand that the same stills are in use by the Pond Extract Company, at the present time. With our new stills, I added about twenty-two and one-half per cent to the strength of the extract.[1]

"There seems to be only two or three sections of the United States where the true species of Witch Hazel grows, of the quality employed by the Pond Company and the Indian 'Medicine Man' of the Oneidas, namely, Central New York and Connecticut. I am told that each year the tribes of Indians on the plains send their Medicine Man East, for their supply of what they term 'Witch Hazel Bush.'

"In 1884, our president, F. W. Hurtt, passed away, and I was elected President of the Company, remaining in that position until I resigned, in 1898. At that time our business was about half a million dollars each year.

"In 1882 I added several new preparations, consisting of toilet cream, dentifrice, lip salve, ointment, porous plasters, catarrh remedy and toilet soap. Special machinery for their manufacture was erected in our laboratory at Number 1 West 13th Street, that building being connected with the one containing our offices, at 76 Fifth Avenue. All the articles above mentioned were made from the product of Pond's Extract, in different forms, and proved very successful with a large trade.

"In 1878 we had opened a branch on Great Russell Street, London, opposite Bridges Museum, and there built up a reasonable trade, principally on Pond's Extract. We also established an agency with Roberts and Co., of Paris, France. We exhibited our preparations at the Paris Exposition, and received a medal. The date of that Exposition I have forgotten,[2] and have no data by which I can recall it. I think the present Pond's Extract Company retains the London Branch, at the present day.[3]

"While in London, I made a contract with the Hotel Syndicate that controlled all the first-class hotels in London. The contract was as follows: The Syndicate to buy from the London Company ten gross of Pond's Extract, of the small size, and pay our regular wholesale price for it. They were to place a bottle in each guest's room, charging same to the room. When occupied by a guest, it was the duty of the chambermaid to report to the office whether or not the guest had used the bottle. If so, it was charged to the guest, and another bottle immediately put in its place. We were to place in the 'lifts' of each hotel a large mirror with the words 'Pond's Extract' lettered across its top. Other mirrors were to be placed in the reception room and the public rooms on the first floor. This would have required an expenditure of ten or eleven thousand dollars. For this privilege, for one year, we were to pay the Hotel Syndicate One Thousand Dollars. However, the Board of Directors of my company refused to sanction my agreement, and the contract was not consummated."

FURTHERING PHARMACEUTICAL PUBLICITY.* THROUGH THE OPEN OR PARTIALLY OPEN PRESCRIPTION DEPARTMENT.

BY W. BRUCE PHILIP.

In many drug stores the prescription department is tucked away. It is out of sight of the customer of the drug store for whom prescriptions are compounded. It is a hole into which his prescription disappears as a piece of paper, and presto, comes back from, as a filled bottle, or pill box. To the average customer the technique that it goes through is analogous to the one of putting a ten dollar bill into one of

[1] Just what Mr. Hurtt meant by the term "Extract," I did not learn. J. U. L.

[2] Probably 1889.

[3] 1915.

* Section on Commercial Interests, A. PH. A., Washington meeting, 1935.

the air cash boxes in a department store, and having it come back turned into silver dollars, nickels and dimes.

The only way that pharmacists are going to convince the public that real manipulation and studied procedure, which require skill, is used in compounding prescriptions is to show the processes. The prescription counter that is seen will be interesting and educating.

Personally, I take a decided stand in advocating the partially open prescription department, regardless of the fact that there are a large number of "one man drug stores" in which the pharmacist is often placed at a disadvantage when he is called away from compounding a prescription in order to serve a customer. If he were working at an open prescription department the fact would, of course, become obvious to anyone in the store, that he had left his work at the prescription counter, to wait upon an incoming customer. The interruption of work for the prescription would be noticeable, but why hide it? I do think, however, that pharmacy must do something to keep its professional rating, and that something must be done at once.

In contacting members of Congress, and other legislators, my experience has been that lawmakers are more and more inclined to classify retail drug stores under the category of "merchandising establishments." Legislators in general are reticent, they are not at all willing to enact additional restrictive legislation which is related to laws dealing with professional pharmacy; they hesitate to even consider giving druggists the right of the exclusive sale of drugs.

To open up the prescription departments, or to give the public a glimpse of this part of the store work, will help to stimulate in the public mind the knowledge that the pharmacist is more than just a merchant. *He is a professional man*, but is not thought of as such.

The processes of filtration, percolation and the manufacturing of certain pharmaceuticals may well be displayed with advantage.

In my opinion, the seeing of the actual filling of prescriptions will have a psychological effect upon both the public and the physician.

We should disregard the fallacy that more prescriptions cannot be written than are now being written, because if the public had full confidence in the ability of pharmacists as professional men, or if there was a trust in the retail drug store the public would demand, and the physician would write more prescriptions.

It is the belief of the writer that the open prescription counter would curtail the dispensing of prescriptions by physicians who make a habit of such a practice. I might even add, that people who now buy patent and proprietary medicines might be interested by seeing the art of pharmacy practiced in a drug store, to induce physicians to write prescriptions for pharmacists to compound. Illegible prescriptions or those for other reasons which require study can be read without attracting the patient's attention. There seems to be no logical reason why a part of the prescription department should not be kept out of view of customers, permitting a certain amount of privacy to the pharmacist who is working out a dispensing problem.

One phase of the case is that there are some untidy prescription departments which the dispenser would be ashamed to have the public see. All right, if a partially open prescription department will clean up for druggists who are careless

dispensers and manufacturers the sooner a partially open prescription department is installed the better it will be for every one concerned and interested in pharmacy.

The writer recommends that a glass partition be so arranged that conversation in the drug store proper cannot be distinctly heard in the prescription department. In like manner the glass would prevent the carrying of voices in conversation from the prescription counter to customers in the store.

In the final analysis, pharmacy is a profession, and pharmacists should act accordingly. Shall the professional part of the drug store, the prescription department, be limited to a number of professional stores, or to hospitals? No! The plan does not appeal to the writer and it is not the public's idea of good *drug store service.* The public wants and needs *drug stores.*

With all facts considered, the drug store is still a drug store, but there is a need to emphasize it. A partial opening of the prescription department to the public's inspection will emphasize the art of the pharmacist, and will give a solid foundation for the demand for legislation in the public interest. There is a virtue and a need to confine the sale of drugs and medicines to qualified registered pharmacists.

ANNUAL MEETING OF THE BOARDS AND COLLEGES OF PHARMACY, N. A. B. P. DISTRICT NO. 2.

The annual meeting of the Boards and Colleges of Pharmacy, N. A. B. P., District No. 2, was held in the American Institute of Pharmacy, March 11th and 12th. The meeting was representative of these bodies and a dinner was given on March 11th to the visiting delegates of the Boards and Colleges under the auspices of the District of Columbia Veteran Druggists' Association, assisted by the D. of C. Pharmaceutical Association, D. of C. Board of Pharmacy, the George Washington University School of Pharmacy and Howard University College of Pharmacy.

Dean C. Leonard O'Connell was chairman for the Colleges and John M. Woodside for the Boards. Reports of the various standing committees were received and discussed. Among the reports were those on examination technique and statistics. Other reports dealt with phases of examinations and experience requirements and on the fate of the pharmacist under socialized medicine.

Other meetings recently held in the American Institute of Pharmacy were those of the Medical Round Table Association and the Chemists' Club.

THE TWELFTH INTERNATIONAL PHARMACEUTICAL CONGRESS.

Among the subjects that will be considered at the Twelfth International Congress in Brussels are the following: The medico-pharmaceutical scope, the limitation of pharmacies, pharmaceutical regulations—control of patent medicines and prices to be charged, management of pharmacies, pharmaceutical service in social insurance, the question of employment in pharmacies, pharmaceutical terms.

AMENDMENT PERMITS RETAIL DRUG CODE AUTHORITY TO INCORPORATE.

The National Industrial Recovery Board on March 20th announced approval of an amendment to the code for the retail trade, permitting the code authority for the retail drug trade to incorporate. The amendment applies to the national code authority and to each local committee.

Written assent of the National Industrial Recovery Board must be obtained before any such code authority may incorporate.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

The following short paper by Dean Spease presented in his characteristic way contains food for thought by all those who are called upon to teach pharmaceutical arithmetic. As one who has had considerable experience in teaching this subject, I want to say that I am indeed happy that the forthcoming Pharmacopœia will eliminate the difficulties we have had in the past in teaching the subject of "percentage solutions."—C. B. JORDAN, *Editor*.

SOME OBSERVATIONS AFTER TWENTY-FIVE YEARS' EXPERIENCE IN TEACHING PHARMACEUTICAL MATHEMATICS.

BY EDWARD SPEASE.*

(CONFERENCE OF TEACHERS OF PHARMACY.)

I have been asked to say a few words upon my observations of twenty-five years in the teaching of Pharmaceutical Mathematics.

This paper will be short even though I might make many observations and it will only be necessary to point out one or two things that are of interest.

Back in the days of the two-year course before students were high school graduates I always found it necessary to drill each class over and over again upon the tables of weights and measures before they were ready to begin any form of mathematics. After that they learned methods and principles and what they learned were largely memory feats. To-day this is not true and one lesson upon the metric system, one upon all others, and one upon conversion is sufficient.

Of course, there is continued use which furnishes repetition and that clinches the memory part, but to-day they are able to confront themselves with mental pictures and weights and measures mean something real to them though they are not as proficient in the multiplication tables as in olden times. This is explainable. May I add at this point, always show them a grain of wheat and point out the origin of the grain and that it represents 64.8 mg.

I read the other day that one of our deans found fault with the high schools. After visiting many high schools I cannot lay the blame at their doors. I find high school graduates to-day lacking in experience. They do not have the experience to draw upon that we older folk have who lived upon farms, in villages or had connections with shops and mechanical devices, if only through our friends. To-day they read of them but don't do them. Riding on a street car or in an auto to school does not furnish that rich background of experience. Shop courses provide much of it but not for all students. This observation also includes the fact that things learned in the grades may never recur until the student reaches us in college and for some, never again. How many of you now know your Latin conjugations and declensions, but review them once more and they will stick.

I enjoy the student of to-day and believe he is easier to teach, and especially since I have visited high schools, read teachers' magazines, talked to high school teachers and learned what they are trying to do.

* Dean, Western Reserve University School of Pharmacy, Cleveland, Ohio.

The subject of percentage solutions, happily, has been solved by a statement in the British Pharmacopœia and by a similar one to appear in our own next revision. Have you read W/W, W/V and V/V of the British Pharmacopœia?

I have only a few more points to mention. The first is the ever-present difficulty in teaching the student to apply what he knows. He always thinks that percentage or any other matter is different in Pharmacy from what it is elsewhere. This is one point at which the teacher's ingenuity is most taxed.

I should like to recommend to you never to accept an answer, either in whole or in part that cannot be weighed or measured. For instance, one cannot weigh odd fractions, have them expressed in weighable and measurable denominations. Our hospital manufacturing laboratory has done much to help us in this regard.

One principle I always follow is to make all first class room calculations with the utmost accuracy and then, later, give problems and teach when "round numbers" may be used. I tell them an educated person should know when to use judgment, and "round number" factors should not be memorized. I have them calculate the variations in dosage of strychnine in five gallons of a preparation by comparing 19 liters with 18.925 liters as the equivalent of 5 gallons.

Should we all "jump through the same hoop," and is it wise to have all our colleges of pharmacy placing the same emphasis upon all courses offered? We all agree that each college should have individuality. There should, however, be a maximum and minimum beyond which it would not be wise to stray. Several times members of the American Association of Colleges of Pharmacy have studied our college catalogs and offered criticisms. Your Editor believes that as we develop the four-year course there will be less and less reason for criticism. The following study by Dr. Burlage is of great interest and his general comments are worthy of careful consideration. I am sorry that space will not permit the publication of the chart that accompanies Dr. Burlage's paper. The faculty of every college of pharmacy should be interested in this study because it gives an opportunity to determine whether their institution is much out of line in the time devoted to and content of the curriculum.—C. B. JORDAN, *Editor*.

A COMPARISON OF THE FOUR-YEAR CURRICULA IN PHARMACEUTICAL SUBJECTS.

BY HENRY M. BURLAGE.*

Beginning with the academic year 1932–1933, the member colleges of this Association entered upon a new phase of educational endeavor with the elimination of all short courses in Pharmacy by requiring the completion of four years of college training before a degree in Pharmacy might be obtained. As we all know this necessary advancement was attained only after years of struggle and effort on the part of educational leaders in pharmaceutical instruction with the hopes that this profession might be put on a higher plane than it has occupied in the past. The writer feels that such hopes cannot be fully realized unless a critical examination of the individual courses making up the new curricula is resorted to with the purposes of bringing about unification of such courses, the elimination of repetitions and obsolete material and a modernization of the same.

Unfortunately the fourth edition of the Pharmaceutical Syllabus, representing

* Professor of Pharmacy, School of Pharmacy, University of North Carolina.

the composite efforts of 21 individuals interested in pharmaceutical affairs and 30 or more teachers recognized in their respective fields, was not released until January 1932 and was, therefore, not available for study in the unification of course instruction.

In order to make a critical examination of the courses in so-called Theoretical and Operative Pharmacy which he offers, the writer decided to study the curricula of the various colleges of the Association to ascertain the position of Pharmacy in these curricula as to time, course content and compare these courses with those outlined in the Syllabus. Accordingly the catalogs for the session 1933–1934 of the member colleges were studied and the results to the best of the author's ability are tabulated in the accompanying table.

This study revealed such non-uniformities that it was deemed advisable to present these findings to the Conference of the Teachers of Pharmacy, to show the need of a critical survey of these Pharmacy courses as to content, time, year offered, etc., with the hope that this Conference might make some definite recommendations to the Association in order to bring about a greater uniformity of catalogs, valuations of didactic and laboratory hours, etc.

Arithmetic of Pharmacy (*Syllabus Requirement* (*Lectures*) *32 + 0 = 32*).—Forty-five of 52 curricula offer this subject under the above title or similar titles. There is a probability, however that this subject matter might be offered in other courses. It is unfortunate that it is necessary for this to be listed in a four-year course. It appears that such a course is necessary since students are so poorly prepared in the fundamentals of arithmetic and algebra that they cannot handle the problems pertaining to pharmacy. The writer feels that the essential work in this subject can be offered without much difficulty in other beginning courses in Pharmacy of a more dignified title. It is pleasing to note that the majority of the schools offer in the Freshman year, only the Syllabus requirement.

Dispensing (*including Incompatibilities*) (*Syllabus Requirement* (*Lectures*) *64* + (*Laboratory*) *128 = 192*).—Practically all of the schools offer courses under this heading; a few, however, list Dispensing under Manufacturing Pharmacy; some offering an unusually large number of hours of Dispensing, probably including other course material. A majority of the schools offer the hours suggested by the Syllabus, or more; 19 schools as far as could be ascertained offer less than the Syllabus requirement in hours. It appears that any school offering less than 192 hours is neglecting an important phase of Pharmaceutical education and that even more than this amount might be desirable. This subject has no place in the curriculum before the Junior year; the survey shows that a majority offer it in the Senior year.

History of Pharmacy (*Syllabus Requirement* (*Lectures*) *32 + 0 = 32*).—Twenty-eight schools offer this course, which might be developed to be of great value in raising the professional morale; some, no doubt, include the subject matter in other courses. A majority offer 32 hours chiefly in the Freshman year. The proper time to offer this material is subject to discussion.

Pharmaceutical Jurisprudence (*Syllabus Requirement* (*Lectures*) *32 + 0 = 32*).—Thirty-three schools offer this material in courses ranging from 11–96 hours; 14 offer the Syllabus requirement; 20 offer the course in the Senior year. It seems appropriate to offer this course only in the Senior year devoting *not more* than 32 hours; also rather than provide for another course of low credit hours, this material might well be covered in a course in Dispensing or Commercial Pharmacy.

Latin of Pharmacy (*Syllabus Requirement* (*Lectures*) *32 + 0 = 32*).—With many students offering several years of Latin as entrance credit, this subject in the writer's opinion is overemphasized and the necessary instruction might be introduced in beginning Pharmacy courses and later in Dispensing when the prescription is studied. Hours range from 16–48 with 22 curricula out of 27 offering 32 hours. It seems appropriate to offer this work in the Freshman year and a majority recognize this fact.

Manufacturing Pharmacy (*Syllabus Requirement—Optional—* + (*Laboratory*) *96 = 96*).—Twelve catalogs offer courses under this title with hours varying from 80–192 in the Junior or

Senior years; lecture work is offered in most cases. There seems to be some confusion as to the content of the course. According to the Syllabus, Manufacturing Pharmacy is "quantity production of pharmaceuticals," or production on a semi-commercial scale and does not mean the preparation of pharmaceuticals in small quantities.

Following Manufacturing Pharmacy, the Syllabus lists in order, Operative Pharmacy ((lectures) 64 + (laboratory) 128 = 192), Pharmaceutical Technique (0 + (laboratory) 64 = 64) and Theory of Pharmacy ((lectures) 192 + 0 = 192) totaling 256 + 192 = 448 hours. The subjects are outlined to include subject matter of the greatest basic and fundamental importance in pharmaceutical training and should receive the greatest study and attention of teachers of Pharmacy. These subjects, no doubt, as outlined in the Syllabus, have and will receive criticism as to content, time allotment, etc. It is unfortunate that these sections were not divided more strictly, stating a time requirement for the various subdivisions, thus avoiding a certain amount of confusion that is evident in a study of the curricula of the schools. This condition has made the tabulation of these vital subjects difficult. In order to simplify this task somewhat the following subdivisions of the three subjects of the Syllabus are adhered to: Pharmaceutical Technique, Galenical Pharmacy, Pharmacy of Inorganic Chemicals, Pharmacy of Organic Chemicals (including New and Non-official Remedies).

Pharmaceutical Technique.—Fifty-one schools offer this subject matter under the above or similar titles with hours varying from 32–320; those offering a large number of hours, however, also include other subject matter. Thirty-four offer the work in the Freshman year; 13 in the Sophomore year; 3 in both years; in most cases lecture work accompanies the laboratory work. It appears that the course in catalogs should be more clearly defined. From the writer's experience, a satisfactory division of hours appears to be ((lectures) 48 + (laboratory) 64 = 112), offered as a Freshman or early Sophomore subject employing in the laboratory work official examples of the processes wherever possible.

Galenical Pharmacy.—While many individuals object to this title, the writer feels it to be distinctly pharmaceutical, indicating a phase of the so-called Operative Pharmacy involving the classes of the official preparations and their manufacture especially those which do not involve chemical reactions. This phase of the work should be regarded by the teacher of Pharmacy as one of the most important of pharmaceutical training. In no other course can the theories of the basic courses be so applied as to develop technique, professional pride and interest. Under no conditions should it be neglected in organization and time.

Fifty catalogs list courses which are distinctly galenical pharmacy; in some cases, technique, inorganic pharmacy, manufacturing and commercial pharmacy are also included. Clock hours vary extremely from 53–544; the subject matter is offered in the majority of cases in the Sophomore year but the spread extends from the Freshman to the Senior years. It appears that a course of 160 hours ((lectures) 64 + (laboratory) 32 = 96) offered not earlier than the Sophomore or Junior year is satisfactory and desirable.

Pharmacy of Inorganic Chemicals (*Inorganic Pharmacy*).—A course with one or the other of these titles is subject to much controversy as some individuals feel that this material falls in the realm of so-called Inorganic Pharmaceutical Chemistry or that it is adequately covered in basic Chemistry courses. To a certain degree the writer concurs with these opinions. A course seems highly desirable which deals with the official inorganic compounds, studying them from the angle of their periodic classification accompanied by laboratory exercises performing the necessary tests and preparing and studying the official preparations involving chemical reactions of these inorganic substances.

Twenty-nine schools offer courses which might be construed to include this course material with a wide variation of hours offered chiefly in the Sophomore and Junior years. A course of 80–96 clock hours ((lectures) 32 + (laboratory) 48 = 80) or ((lectures) 32 + (laboratory) 64 = 96) offered in the Sophomore year seems desirable.

Pharmacy of the Organic Chemicals (*Organic Pharmacy*).—Such a course is also subject to discussion especially as to course content since it might be included in so-called Organic Pharmaceutical Chemistry. The writer does not agree with these contentions especially if the Pharmaceutical Chemistry courses are of a basic nature since the fundamentals of organic chemistry cannot be stressed and at the same time a study of the official organic compounds be made; some knowledge of the more complex substances of natural origin and especially the ethical new and

non-official remedies which are becoming more and more important should be stressed. A course of 48–80 hours ((lectures) 48 + 0 = 48) to (lectures) 48 + (laboratory) 32 = 80) offered in the Senior year would be especially valuable.

Commercial Pharmacy.—Thirty-four catalogs listed courses which vary greatly in hours and offered chiefly in the Junior or Senior years; such courses are not offered by some schools since the commercial subjects are offered in service departments as Economics and Commerce.

GENERAL COMMENTS.

1. Of the 54 catalogs studied, 53 offer curricula for the four-year course.
2. Eleven of the 54 colleges are on a quarter basis.
3. The curricula of 11 schools offer too many courses of small credit evaluation. This weakness can in part be corrected by uniting the didactic course with the laboratory course in the same subject, rather than offering two courses. This has been an outstanding weakness of Pharmaceutical curricula for years and presents a condition which is open to much criticism by educators. A course requiring only one lecture hour a week should be increased in credit value or incorporated with a suitable major subject where it might be treated appropriately.
4. Four curricula offer Seminar courses which is of questionable value for under-graduates unless they have unusual ability.
5. Five institutions offer Assaying in pharmacy courses. This instruction seemingly and more properly should be offered in Quantitative Pharmaceutical Chemistry.
6. Considerable variation as to the number of laboratory hours equivalent to 1 credit hour is apparent. Nine curricula listed laboratory courses with no credit for this work to 1, 2, 3 and 4 clock hours equivalent to 1 credit hour.
7. Three colleges offer courses in the Use of the Library and Literature; such subject matter might well be offered in History of Pharmacy.
8. A course entitled Research and Thesis offered by 3 schools is of a commendable type but it appears that it should be offered as an elective only to those undergraduates who possess unusual investigative ability.
9. Pharmacy courses are distributed throughout the four years by most of the institutions with the following exceptions: one school with no work in the Junior year, two with none in the Senior year, and six with no work in the Freshman year.
10. Twenty-three curricula list one or more courses which to all appearances are review courses preparatory to the State Board Examinations. Such review seemed advisable when 2- and 3-year curricula were offered but in the new curriculum seems unnecessary with the additional time allowed and if the courses offered are of such a calibre and so distributed as to allow more intensive and thorough study. The time consumed by review courses might well be devoted to courses elective for the purpose of broadening the training of the student.
11. Curriculum Outlined and Course Descriptions.

(*a*) In 9 catalogs didactic and laboratory hours not stated in whole or part.
(*b*) Eleven offer vague or confusing course descriptions and outlines; 5 of which were difficult to study intelligently.
(*c*) Two outlines of study with no course numbers.
(*d*) One with credits poorly defined.
(*e*) Credits in 2 curricula outlines did not correspond with those in the course description.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

BALTIMORE.

The February meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Hotel Emerson on Monday, February 18, 1935. President Wm. F. Reindollar presided.

The speaker of the evening was Dr. J. Leon Lascoff,[1] of New York City, who discussed methods of compounding difficult prescriptions and gave demonstrations. The title of his paper was—"It Can Be Done"—the paper follows:

IT CAN BE DONE. III.

The author stated that this was the third paper of the series, the first was presented at the Baltimore meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, and the second before the Massachusetts Pharmaceutical Association.

The presciptions discussed in this paper are representative of those received in the "Lascoff Pharmacy," some are brought in by pharmacists to be compounded for them, on others advice was asked by phone and otherwise.

Requests are received daily from pharmacists asking for advice in dispensing. Quite often, the reason for this is due to the fact that the patient has brought in a copy of the prescription from another pharmacy. The one who originally compounded the prescription may have dispensed a clear solution or a homogeneous mixture. The next dispenser may have produced a cloudy mixture, or one so unsavory that the patient probably felt that he would be benefited more by not taking it than by following the directions on the label.

Such differences in results of dispensing often lead physicians to prescribe proprietaries. It is not difficult to understand why; the physician is certain, to a degree, that when he prescribes a proprietary that he will obtain a mixture containing equally divided doses, having a pleasant taste, a good color and a uniformity of appearance no matter where it is dispensed.

The New York State Pharmaceutical Association has appointed a U. S. P. and N. F. Propaganda Committee, which has sponsored meetings of physicians and pharmacists. At these gatherings the physicians have been asked why they did not prescribe U. S. P. and N. F. preparations more frequently. The gist of their complaints was the lack of uniformity in dispensing and the fact that they could not obtain satisfactory preparations of the same medication from different pharmacists.

It was pointed out, of course, that if the patient read the prescription, and discovered that the medicine was a proprietary which could be purchased practically anywhere, it was very apt to

[1] Chairman, Committee on Recipe Book.

lead to self-medication. Most physicians are willing to prescribe official preparations if they can do so with the assurance that their patients will receive uniform, palatable preparations.

Physicians are visited daily by detail men from the pharmaceutical manufacturing houses. Usually samples of proprietaries and the "Pharmacopœia" of the manufacturer are left with the physicians. The question arises, "Why does not the Pharmacist do his own detail work?" There are many practical methods of doing this, and the results are really worth while.

If all pharmacists belonged to, and supported the state and national pharmaceutical associations, effective propaganda could be carried on, the purpose of which would be to acquaint physicians with the merits of official preparations and the advisability of prescribing them.

Unfortunately, many pharmacists have no desire to develop their prescription practice; they consider it a "necessary evil." They prefer selling some article which merely requires wrapping up; they consider that this type of business is easier to handle, requires less work, involves no responsibility and the profits are greater. But prescription business is worth while, and statistics prove it.

Quoting Dr. Robert L. Swain, in a recent issue of *Drug Topics:*

"Statistics reveal that retail pharmacists compound annually more than 250,000,000 prescriptions. Each of these represents a contribution to the health and physical welfare of the general public. This impressive record establishes the pharmacist as a health officer whose profession is vitally affected by the public interest."

Mind you, 250,000,000 prescriptions are compounded in the course of one year! This figure offers a very obvious answer to the question, "Is prescription business worth while?"

For years the separation of the pharmacy from the drug store has been advocated by the speaker—the professional pharmacy should not be submerged by side-lines, and sandwich counters, and it is interesting to note that for the past few years there has been a definite movement toward professionalism in pharmacy. Many pharmacists who had luncheonettes which practically obscured their prescription counters, have discarded the lunchrooms and are featuring prescription departments instead.

In the writer's observations of these changes he has noticed three types of Prescription Departments for which improvements might be suggested:

1. The type which is entirely enclosed, which is tucked into a very small space in the pharmacy, and bears a "No Admittance" sign.

2. The type having a partition so high that persons on the outside can see only the ceiling of the prescription room.

3. The type having the entire prescription room open to the view of the public. Everything the pharmacist does is seen by the customer. This is not always advisable.

The writer does not approve of prescription rooms which are too open nor of those which are entirely closed. There should be a happy medium—neither completely closed nor entirely open. The dividing partition between the prescription room and other section of the pharmacy should be high enough for a person to see the head of the pharmacist at work, but not his hands. The patient should not see when a label is washed off a bottle or when pills are transferred from an original package to a box, in order to affix directions.

In the average store the size of the Prescription Department should be about one-third that of the entire store. The counters of the department should be made of "white glass." This is very easily kept clean and presents a very attractive appearance to the laity who observe; it also makes a good impression on physicians who are enthusiastic about cleanliness.

Needless to say, it is not enough to just install an attractive prescription room; pharmacists cannot stop at this point—they must make their departments pay.

There are many methods which can be used to increase the volume of the prescription business:

Detailing the neighborhood physicians advisable.—Let the physician know that you are equipped to help him solve his prescription problems. Impress him with the idea that you can do something for him. Interest him enough so that he will visit your pharmacy and your prescription department. But be sure that you have something worth showing, so that the physician will not feel that his time has been wasted.

Keep the public advised of the fact that yours is a professional pharmacy. Advertising in

the local papers and journals is an effective method of doing this. Well-arranged, professional windows usually attract attention and create a lasting impression.

In dispensing, use neat boxes, labels and wrapping materials. Everything that leaves the pharmacy must be in tip-top order. Use only those ingredients manufactured by reputable concerns.

In the writer's opinion a successful prescription pharmacy cannot be run by one man alone; a prescription should be compounded without interruptions. This is not possible when one man attempts to take care of both the counter trade and the compounding. The pharmacist should be able to carefully read over the prescription, noting the doses, and the incompatibilities if any are present. Under no circumstances should he be that type of pharmacist who continually abuses the "Shake Label." If he is in doubt about any of the ingredients in a prescription or about the doses he should consult the physician or reference books. Those prescriptions which present compounding difficulties should be studied with care. Many mixtures from which it is, at first glance, seemingly impossible to make a palatable, homogeneous preparation can be properly made and dispensed with the exercise of due thought and care.

The prescriptions which follow are samples of those which have troubled many pharmacists. Correct compounding procedures have converted them from disagreeable looking, unsatisfactory products, to preparations which are proper and correct for administration as medicine.

℞ 1	Ichthyol	4.0
	Calamine	8.0
	Zinc Stearate	2.0
	Lime Water *q. s.*	120.0

In compounding this prescription, as written, the zinc stearate will float at the top of the mixture. Neither acacia nor tragacanth will help in obtaining a smooth mixture. The only remedy is to add glycerin to the zinc stearate, rubbing well. Add the calamine. Add the ichthyol previously dissolved in a small quantity of water. Finally add lime water enough to make 120 cc.

℞ 2	Potassium Iodide	ʒI
	Salicylic Acid	ʒII
	Sodium Bicarbonate	ʒII
	Tincture of Colchicum Seed	ʒIII
	Aromatic Elixir	
	Compound Syrup of Sarsaparilla of each *q. s.*	fʒIII

This prescription does not contain sufficient sodium bicarbonate to neutralize the salicylic acid. It is necessary to add 2 drachms of sodium bicarbonate to the salicylic acid with the aromatic elixir. When the reaction has taken place, filter out the excess sodium bicarbonate and add the other ingredients. The resulting solution is clear without any sediment or precipitation.

℞ 3	Ammoniated Mercury	2.0
	Acid Salicylic	3.0
	Phenol	0.5
	Alcohol*	15.0
	Soft Soap	10.0
	Rose Water *q. s.*	90.0

The pharmacist who presented this prescription complained that after compounding, a heavy lumpy precipitate formed which greatly resembled a sponge. No matter how he attempted to fill this prescription, he did not get a satisfactory preparation. The method used in the preparation shown, was to rub up the ammoniated mercury and the salicylic acid to a very fine uniform powder. Add the rose water, triturating well until a smooth paste is formed. Add the soft soap and lastly the phenol.

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* The alcohol was omitted, because this seemed to cause all of the trouble.

℞ 4	Zinc Sulphate	gr. I
	Boric Acid	gr. V
	Sodium Borate	gr. IV
	Rose Water *q. s.*	fl. oz. I

This prescription is intended as an eye prescription and if compounded as written will form a zinc borate compound which is insoluble. The addition of Price's Glycerin does not dissolve the precipitate sufficiently to enable it to be used in the eyes. The only other alternative is to filter, which was done.

℞ 5	Betanaphthol	ʒI
	Asafetida	ʒII
	Syrup	fʒII
	Elixir of Three Bromides *q. s.*	fʒIII

The pharmacist telephoned in this difficult prescription and informed us that he had tried making an emulsion using acacia to emulsify the asafetida. He evidently did not remember that there is an official Emulsion of Asafetida, which does not employ acacia or tragacanth. We rubbed up the asafetida to a very fine powder and then adding water very little at a time, formed an emulsion. To this add the betanaphthol previously rubbed up with the elixir of three bromides and add the syrup. This mixture was strained through cotton. The result is a homogeneous mixture without any separation.

℞ 6	Morphine Sulphate	gr. II
	Potassium Iodide	gr. C
	Tincture of Belladonna	ʒII
	Peppermint Water *q. s.*	fʒIII

When compounded, a precipitation of morphine alkaloid takes place due to the action of the potassium iodide on the alkaloidal salt, morphine sulphate. There is not enough alcohol in the tincture of belladonna to keep the morphine alkaloid in solution, therefore it is necessary to add about three drachms of alcohol, which will dissolve the precipitate.

℞ 7	Cinnabar	4.0
	Precipitated Sulphur	4.0
	Water *q. s.*	120.0

This prescription presented a very messy appearance when compounded as written. The cinnabar stuck to the sides of the bottle and could not be shaken into a uniform mixture. It is not necessary to use acacia or tragacanth. In preparing this prescription, we rubbed up the cinnabar with half an ounce of glycerin and added to this the precipitated sulphur. Finally, the water was added, forming a fine uniform homogeneous mixture without any messy separation.

℞ 8	Fluidextract of Cannabis	ʒIss
	Ammonium Chloride	ʒIII
	Syrup of Hydriodic Acid *q. s.*	fʒIV

The resins of cannabis will be precipitated out by the syrup, therefore, it will be necessary to add an equal amount of acacia to the cannabis. Dissolve the ammonium chloride in about three drachms of water. To this add the syrup of hydriodic acid and add gradually to the fluidextract of cannabis and acacia. The resulting mixture does not contain any precipitation and is a uniform mixture, suitable for dispensing.

℞ 9	Lead Acetate	4.5
	Precipitated Sulphur	4.5
	Glycerin	4.5
	Water *q. s.*	90.0

In this prescription the sulphur will separate out and a uniform mixture cannot be obtained if compounded as written. It is necessary, therefore, to rub up the sulphur with a drachm of tragacanth, to which glycerin was added. Dissolve the lead acetate in water and add to the sulphur mixture. Finally add enough water to make the ninety cc. This mixture, when shaken, is presentable and can very well be dispensed without fear of the sulphur separation taking place.

℞ 10	Sodium Borate	9.0
	Oil of Gaultheria	3.6
	Liniment of Soft Soap *q. s.*	120.0

We compounded this prescription as written and noted after a while that there were large pieces of floating borax (presumably). This was also evidenced when the lotion was rubbed on the hand. It was very gritty. To remedy this, we dissolved the sodium borate in a small quantity of hot water and rubbed this up with soft soap. Next we added the oil of gaultheria and the liniment of soft soap, enough to make 120 cc.

℞ 11	Sodium Bromide	ʒIII
	Ammonium Bromide	ʒIII
	Elix of Iron, Quinine and Strychnine Phosphate *q. s.*	fʒIII

The elixir is not very stable and is incompatible with a large number of other ingredients. In this prescription it is advisable to use the Elixir of Iron Quinine and Strychnine Citrate. The solution would then be clear without any separation or precipitation.

℞ 12	Potassium Chlorate	8.0
	Tincture of Myrrh	12.0
	Distilled Water *q. s.*	120.0

This is intended as a gargle but could not be used if compounded as written. There is a separation of the constituents of the tincture of myrrh when added to the water. To overcome this, we rubbed up the tincture of myrrh with one drachm of powdered acacia. Separately we dissolved the potassium chlorate in some water and added to the myrrh and acacia. Finally enough water was added to make the 120 cc. The final mixture is homogeneous without any separation.

℞ 13	Strontium Bromide	12.0
	Ammonium Carbonate	8.0
	Syrup of Tolu	30.0
	Water *q. s.*	90.0

The difficulty in this prescription lies in the fact that the strontium bromide is incompatible with alkalies. Therefore, it is necessary to use ammonium bromide in place of the strontium bromide when a very nice clear solution results.

℞ 14	Phenobarbital	0.5
	Sodium Bromide	4.0
	Elixir Pyramidon	45.0
	Water *q. s.*	60.0

When compounded, we noticed a precipitate of fine crystals which probably is the phenobarbital. Instead of using phenobarbital, we used the soluble phenobarbital, namely—Phenobarbital Sodium. We dissolved this together with the sodium bromide in water and added the elixir pyramidon. There is not sufficient alcohol in the elixir to precipitate out the phenobarbital sodium.

℞ 15	Menthol	0.06
	Camphor	0.06
	Mercurochrome	0.12
	Olive Oil	60.00

The mercurochrome is not soluble in the olive oil; therefore, it is necessary to dissolve the mercurochrome in a few drops of water. Pick up this solution with a small quantity of Aquaphor. To this gradually add the olive oil. In another mortar triturate the menthol and camphor together until they liquefy. Add some of the olive oil to this. Finally, mix both solutions and add enough of the oil to make the two ounces. The resulting mixture does not have any separation of the mercurochrome and is perfectly uniform.

℞ 16	Arsenic Trioxide	0.06
	Extract of Nux Vomica	2.00
	Quinine Sulphate	0.60
	Peppermint Water *q. s.*	240.00

None of the powder ingredients are soluble in water; therefore, if compounded as written, the patient may very easily take an overdose. In preparing this prescription, we used 100 minims of the Liquor Acidi Arsenosi which is 1% arsenic trioxide. Also, instead of using the insoluble quinine sulphate, we could use the soluble quinine bisulphate. Dissolve the extract of nux vomica in some diluted alcohol. Add all of the solutions and then add sufficient peppermint water to make 240 cc. You will note, in the finished product, that there is no precipitation and that the solution is perfectly clear.

℞ 17	Camphor	4.00
	Salicylic Acid	0.66
	Precipitated Sulphur	6.50
	Lime Water *q. s.*	120.00

When compounding this prescription as written, we noticed a complete separation of the insoluble material. To properly compound this we dissolved the camphor and salicylic acid in a small quantity of alcohol. Rub up the sulphur with about a drachm of tragacanth, adding the lime water. Finally mix the camphor solution to the sulphur and add enough lime water to make 120 cc.

℞ 18	Phenol	1.0
	Tincture of Iodine	1.0
	Mucilage of Acacia	4.0
	Alcohol	20.0

When compounded as written, a stringy precipitate results which is due to the incompatibility of the alcohol with the acacia. Therefore, in order to dispense a presentable solution, we can leave out the troublesome mucilage of acacia and the result will be a clear solution.

℞ 19	Iodine	gr. I
	Ephedrine Alkaloid	gr. V
	Menthol	gr. III
	Camphor	gr. III
	Liquid Petrolatum *q. s.*	f℥I

When the pharmacist compounded this prescription, he noted that upon the addition of the ephedrine alkaloid, the solution turned a murky brown and after a day, decolorized completely. This was due, of course, to the action of the alkaloid on the iodine. We compounded this prescription by rubbing up the camphor and menthol until liquid, then added the iodine and a small amount of petrolatum and rubbed until the iodine dissolved. Using ephedrine sulphate instead of the alkaloid, we dissolved this in a small quantity of water and picked it up with aid of Aquaphor. To the ephedrine mixture, we added slowly the liquid petrolatum. Next we added the camphor menthol iodine solution. You will note that the finished product has kept its color and odor of iodine.

℞ 20	Biniodide of Mercury		gr. Iss
	Tincture of Iodine Potassium Iodide Syrup of Ferrous Iodide	of each	℥II
	Aromatic Elixir		f℥II

℞ 21	Magnesium Oxide	ʒII
	Bismuth Subcarbonate	ʒI
	Sodium Bicarbonate	ʒIII
	Calcium Carbonate	ʒII
	Water *q. s.*	fʒIV

This prescription, after standing for a very short time, became very hard and could not be removed from the bottle. When we compounded this, we added to the powders half an ounce of glycerin and this served to keep the powders in sufficient suspension to be dispensed.

CAPSULES.

Recently, the manufacturers have been detailing the physicians on capsules, instead of tablets and pills. This is because of the fact that the physicians are not prescribing ready made pills—they prefer to have the pills freshly made.

The manufacturers are selling such items as Iron and Ammonium Citrate capsules, Digitalis capsules, etc. The cost to the pharmacist is a great deal more than if he were to prepare these himself.

It is not too difficult for any pharmacist to prepare any number of quinidine capsules.

In connection with quinidine, it was called to the writer's attention, the other day, that a physician wrote for "Quinoidine" and the pharmacist dispensed quinidine. Evidently the pharmacist did not trouble to look in his reference books to see if there was such an item as "Quinoidine" or he misread it as "Quinidine."

℞ 23	Quinoidine Capsules	gr. V
℞ 24	Quinidine Capsules	gr. V
	Iron and Ammonium Citrate Capsules	0.5

SUPPOSITORIES.

℞ 25	Chloral Hydrate	gr. X
	Make 12 suppositories.	

The pharmacist endeavored to prepare these suppositories but found that they melted while he was working.

In conclusion the author expressed the hope that the demonstrations had been of interest, and that some of the suggestions offered may prove of value. He said that to him Pharmacy is not just a business; he found it an interesting, and absorbing profession, as well as a hobby. He expressed his appreciation of the efforts in his behalf and thanked the members.

An informal dinner was given for the guest of honor which was attended by members of the Baltimore Branch.

Prof. E. N. Gathercoal,[1] of Chicago, was present and commented on the paper. A general discussion was entered into regarding the presciptions considered by the author. A rising vote of thanks was tendered the latter for his excellent paper.

About forty members attended the meeting.

C. JELEFF CARR, *Secretary-Treasurer.*

CHICAGO.

The monthly meeting of the Chicago branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held February 19th, at the University of Illinois College of Pharmacy.

The speaker of the evening was E. E. Swanson, of the Eli Lilly Research Laboratories, who discussed "Physiological Testing."

An introduction to the discussion was made by mentioning the purpose and uses of bio-assays. Bio-assay, or physio'ogical testing, is used where the chemistry of the drug is not definitely known and where a reliable basis of standardization is needed. With some of the drugs that are bio-assayed there are cases where there are more than one active constituent.

[1] Chairman, Committee on National Formulary.

The speaker cited a cardiac stimulant as an example of bio-assay. These drugs are assayed on the frog or cat. In large production work accuracy of the tests is accomplished by a definite system of procedure. Digitalis, for example, comes to the manufacturing house in carload lots. The crude drug is assayed biologically and must assay at least 10 per cent above the U. S. P. standards. The crude drug is passed if it is satisfactory. Then the various preparations of the drug are returned for further testing.

Mr. Swanson stated that his tests showed the U. S. P. frog method and Hatcher Cat method to give about the same results, but preferred the frog method inasmuch as the cat method would involve the use of about sixty cats per week in the large laboratories.

Aconite was discussed and it was stated that the physiological test for strength was much more accurate than the chemical test, especially after the preparation of the drug has stood for some time. Hydrogen-ion concentration control was mentioned as a means of preventing deterioration.

A discussion of the assay work on ergot, insulin and pituitary extract was made.

Following the discussion lantern slides were shown to demonstrate many of the points that Mr. Swanson had discussed.

LAWRENCE TEMPLETON, *Secretary.*

NEW YORK.

The February 1935 meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in the building of the College of Pharmacy, Columbia University, on the evening of February 11th. About sixty members and their guests attended.

President C. W. Ballard was in the chair and called upon the secretary for his report. This was read and accepted.

Chairman R. S. Lehman of the Committee on Education and Legislation presented his report as follows:

National Legislation.—The new alcohol regulations are out—druggists may buy alcohol in larger quantities than one gallon according to bulletin No. 170 of the F. A. C. A., dated January 22, 1935. This bulletin defines the Industrial Uses of Alcohol as follows:

Use of Alcohol and other distilled spirits or wine in the manufacture of medicinal, pharmaceutical or antiseptic products including prescriptions compounded by retail druggists, of toilet products, of flavoring extracts, syrups or of food products, or of scientific, chemical, mechanical or industrial products, provided such products are unfit for beverage use.

Congress has before it 6000 bills, many of them pertaining to the problems of the retail druggists. Among them three food and drug bills, *viz.:* Copeland S. 1944, McCarran, S. 580, also Hoge, H. R. 3972. No public hearings have been arranged thus far on any of the measures introduced as substitutes for or amendments to the Federal Food and Drugs Act, as the Committees on Interstate and Foreign Commerce will be busy with a number of other important matters.[1] Senator Copeland is seriously considering the amendment of his own bill as to the multiple seizure provision. If so, revised multiple seizures will be dispensed with in misbranded articles. W. G. Campbell, director of the Food and Drugs Administration favors the Copeland bill as covering all points to the satisfaction of both sides.

Senator Copeland recently introduced a bill, permitting the sale of drugs, medicines and other products for the prevention of conception by doctors and druggists, but prohibiting the advertising of such items.

Congressman Treadway of New York introduced H. R. 1424, calling a $2^1/_2$-general sales tax: the administration does not support this measure at present, however; if passed it would realize about twenty million dollars on drug store items alone.

The Federal Trade Commission recently recommended the amendment of Section two of the Clayton Act, making it unlawful to discriminate between purchasers unfairly or unjustly, in other words forbidding quantity discounts, and allowing the small buyer to purchase goods at the same price as the large distributor. A bill introduced by Sen. Wheeler of Montana, S. 944 covers this. It is favored by the N. A. R. D.

The hearing on the Price Fixing provisions of the NRA Codes was held on January 12, 1935. Eighty speakers were heard. All those representing industries were agreed that selling

[1] Hearings were held March 2nd and 8th.

below cost was one of the worst features of the depression. Chairman Williams of the NRA recommends the extension of the NRA in its present form for one to two years more. President Roosevelt is expected to indicate his desires in that respect to Congress shortly.[1]

The N. A. R. D. is making propaganda for a National First Aid Week, in which the necessity of knowing first aid methods and having the materials on hand is impressed on the public. How this will work out in larger communities, where hospital facilities are convenient, and where, as in New York, the rendering of first aid by a pharmacist is more or less frowned upon by the medical profession as practicing medicine illegally is a question.

State Legislation:—The New York State Board of Pharmacy has issued a bulletin publishing its interpretation of the two Dunkel bills recently passed by the Legislature (1934).

It forbids the sale by non-pharmacists of a large number of popular proprietaries. These must be sold in a licensed pharmacy or drug store, by a licensed pharmacist or druggists or under their supervision:

"Group I, eleven items containing acetanilid, acetphenetidine, etc., including various headache powders, effervescent analgesics, etc.

"Group II, twenty-nine items containing poisonous ingredients such as strychnine, arsenic, morphine, etc., and would bar a number of cough medicines and pills similar to Iron Quinine and Strychnine, or Alcin, Belladonna and Strychnine, etc.

"Group III, ten items in the so-called Habit Forming Group, such containing Barbituric Acid derivatives, etc.

"Group IV, eighteen items of various proprietaries which contain such potent ingredients as thyroids, ergot, cincophen belladonna, etc.

"The New York State Pharmaceutical Association through its Committee on Legislation is sponsoring a bill in the State Legislature, this session: A Fair Trade Bill (same as the junior Capper-Kelly Bill now a law in California). The California law has worked to great satisfaction in California: same is indicated by the graphs recently set up by the *Druggists Circular* in New York, showing sales in California at no profit being only $2^1/_2$ per cent of the total in drug stores, while in New York City they represent nearly $33^1/_3$ per cent of the total sales.

"An attempt will also be made to amend the Pharmacy Law defining unethical or unprofessional conduct, and to make them cause for revocation of Pharmacists License."

Following Chairman Lehman's report President Ballard called upon Chairman Stieger of the Progress of Pharmacy Committee for his report; it follows:

In the February 1935 No. of *Industrial & Engineering Chemistry*, Dr. Oser of the Food Research Laboratories of New York City criticizes the Interim Revision of Text for U. S. P. Cod Liver Oil.

The critique is concerned chiefly with the new procedures for biological assay, but the author also objects to the definition and the tests for identity and purity, and to the fact that the only ingredients whose addition to Cod Liver Oil is sanctioned are certain flavoring substances, anti-oxidants being excluded. He states that, among the tests for identity and purity, methods are conspicuously lacking for determination of sophistication by addition of highly potent vitamins containing substances such as halibut liver oil or viosterol.

Chairman E. Fullerton Cook replies for the committee, stating that the text is a necessary compromise. He points out that the text applies only to interim revision and that the new Pharmacopœia will appear shortly. In regard to anti-oxidants, he states that the committee declines to accept responsibility for permissive use of such substances on which so little information is available, particularly with regard to physiological action, and also defends the procedure of the biological assay. Chairman Cook says, "The committee accepts the compliment implied by Oser in suggesting that it provide methods for the detection of sophistication but is forced to admit that it is not in a better position to supply such a method than is the critic."

The January 1935 issue of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION makes announcement of Interim Revision No. 3, a new Ergot Assay. It will become official and enforceable, May 1, 1935.

M. F. Lauro in *Oil & Soap* (Vol. 11, No. 12 (1934)) discusses adulteration of Olive Oil. He states that 10–20% of other oils can be mixed with olive oil before any change occurs in the

[1] He has reported.

constituent limits, which gives evidence of adulteration. In his opinion, present analytical values should be revised.

Caro and Giani in *Zeitschrift für Physiologische Chemie* (1934) found that tissue extracts inhibit oxidation of ascorbic acid (Vitamin C) which is easily oxidized by atmospheric oxygen. Ringer solution and its most important salt constituents in 0.1-M. concentration are likewise inhibitory.

Parsons in *Proceedings of the Royal Society of Medicine* (1934) reports that a case of infantile scurvy was cured by the use of ascorbic acid. This is believed to be the first cure so attained.

The outlook for enteric medication looks quite hopeless. According to "A Study of the Emptying Time of the Stomach with Reference to Pills and Tablets" by Bukey and Brew in the December JOURNAL A. PH. A., tablets may remain in the stomach of the same individual (at various times) from one to more than four hours.

Several conclusions were drawn from their studies of enteric coatings:

1st, that size and shape of pill, tablet or capsule have no effect on length of time it will remain in the stomach

2nd, the same individual does not react uniformly, etc.

3rd, emptying time may be influenced by diet

4th, type of coating does not have any effect, etc.

Chairman Ligorio, of the Membership Committee had not had sufficient time to begin the work of his committee and was, therefore, unfortunately unable to report.

Two letters from President Robert P. Fischelis were then read in which he thanked the New York Branch and Dr. H. H. Schaefer for the testimonial dinner in his honor on January 29th.

The business part of the meeting being over, President Ballard called upon the guest speaker of the evening, Dr. David Bryce, who spoke on Medicinal Dyes. The address follows:

MEDICINAL DYES.

BY DAVID A. BRYCE, M.D.

"Most of you, I feel sure, have had considerable experience of a conversational nature with doctors. Perhaps I am not betraying any professional secrets when I say that your experience has probably been largely that of auditors in such conversations... With your permission, I shall restrict this address to six medicinal dyes.. I feel sure that such technical information may be of direct benefit in your relations with your physician clients, and if I may be permitted to do so, I should like to digress a moment at this point to illustrate why.

"About fifteen months ago, one of the senior executives of my organization requested me to look into certain fundamental economic aspects of medicine, not only in its relation to commercial companies such as our own, but the inter-relationship between physicians. It is unnecessary to bore you with all the ramifications of that investigation which I pursued for several months at odd times, but there were two illuminating results which I pass on to you as of interest in the present discussion. Among other things, I sent out a questionnaire which was very carefully and intelligently answered by the majority of physicians. When we had compiled the results of this questionnaire, we were somewhat amazed to find that there was a feeling of great antagonism, amounting almost to actual hostility, on the part of almost all of the replying physicians toward the retail pharmacist. This was so striking that in my journeyings about the country, I inquired of as many physicians as practicable, and in particular of certain physicians who I knew had answered the questionnaire, as to just why they felt as they did. While it would be presumptuous for me to draw final conclusions from any such very brief and narrow investigation, nevertheless, one cannot help making some deductions or guesses. It appeared to me that the antagonism to which I have referred was due to the feeling by the physician that the retail pharmacist was allowing his interests to become so diversified in the field of commercial retailing to the laity, both of medical and nonmedical supplies, that not only did the retail pharmacist fail to act in the best interests of his physician clients, but that his information on technical subjects, upon which physicians rely, was becoming exceedingly thin. Now please do not misunderstand me, and consider that I am saying that this *is* so. I merely suggest that it appeared to me that physicians think it is so, which may not be the same thing. Criticism in life is seldom just: it is more frequently

biased and reflective of the critic's state of mind than of the fault of the one criticized. At the risk of seeming discourteous to you I have mentioned this to-night because it has appeared to have a bearing on such technical information as I am going to give in this brief address. Should you find it worth while to acquire highly technical, medical and chemical information of this type not only from me but from other medical directors and other persons who happen to be technically informed in special fields, it would appear likely that your acquired knowledge in such fields must inevitably be of use to your physician clients in their every-day contacts with you. Such usefulness must inevitably redound to your own benefit by promoting a greater feeling of cordiality between pharmacist and physician. Perhaps this is far-fetched, but at any rate I leave the suggestion with you for you to assay its worth. Now let us return to our subject.

"What are dyes? It is almost impossible to answer this question in such a way that the definition is universally applicable. A famous definition of a dye is that given by one of our Vice-Presidents in a Customs Court case many years ago. He said that a dye was a substance having a definite affinity for animal or vegetable fibres and which in expressing that affinity, colored those fibres with the color of the dye. Let me illustrate what he meant. Imagine that I have here a cylinder of coffee and that into that I dip a cotton towel and then remove and dry the towel. It is true that the towel will be stained with the coffee, but coffee is not a dye, for if one inspects carefully the remaining coffee solution, it will be seen that the color of that solution has not changed, and that the color deposited in the towel is only that amount of color which ordinarily is carried into the fibres by the solution. In other words, coffee has expressed no affinity of its yellow color for the cotton fibres. On the other hand, if I had here a cylinder containing a weak solution of Tartrazine Yellow and dipped into that a cotton cloth and removed and dried the cloth, not only would the cloth be stained yellow, but the weak solution would have become almost colorless because of the affinity of the yellow color for the fibres which had been immersed therein. Thus you see there is a fundamental distinction between the two processes. The Tartrazine is, of course, a dye. Unfortunately, however, the definition will not stand up under severe cross-examination by opposing counsel in a court of law. One must qualify any definition made. Suffice it to say for our purposes here this evening that a dye is in most cases an organic material containing the benzene nucleus or some ring structure, that is colored in aqueous solutions, and which color has an affinity for animal and/or vegetable fibres.

"What is a medicinal dye? A medicinal dye is one of the very, very few members of the dye series which by practical experience, and solely by such practical experience not by any theorizing—has been found to be of use in the treatment of human disease. The six medicinal dyes with which we are particularly concerned tonight are as follows: Methylene Blue, Crystal Violet, Neutral Acriflavine, Brilliant Green, Scarlet Red Sulphonate and Medicinal Fuchsine. A little later I shall show you some slides illustrating these dyes, together with slides of practical work which has been done in one of the fields of dye therapy, and at that time it will be easier for me to demonstrate the chemical formulas than to try to describe them now.

"A description of medicinal dyes would certainly be incomplete without some mention of their early history. As in the case of almost every synthetic organic chemical, commercial development and scientific development have proceeded, if not actually hand in hand at least closely associated. One of the first artificial dyestuffs, if not actually the first ever made, was Picric Acid or Symmetrical Trinitrophenol, $C_6H_2OH(N_2O)_3$, prepared in 1771 by Woulfe from indigo and nitric acid. Nearly a century later a technical method was developed for the separation of picric acid from coal tar. The dye industry has been largely an outgrowth of that discovery, subsequently various colors such as mauve, magenta, rosaniline blue, Hoffmann's violet, aniline black, methyl violet, methyl green, and many others were discovered and commercially manufactured in England and France. At the same time that this dye research was proceeding, scientific research in pure science was likewise being carried forward and Kekule gave the world his epoch-making hypothesis as to the structural formula of the benzene nucleus. It is unnecessary for me to burden you with all the steps in the development of the synthetic dyestuff industry, but it is interesting to note that between the years 1890 and 1911, the commercial development of dyes for technical purposes becomes a race not only between rival concerns, but between the laboratory and the manufacturing plant. The rivalry was frequently expressed in international terms, but Europe was far ahead of the United States at that time. Great companies such as Badische, Meister, Lucius & Brüning, Griesheim Elektron, and others were constantly producing new and

better dyes or intermediates. The extraordinary capability of the German people for methodical and patient research was peculiarly adapted to the development of dyes. Accordingly, Germany had forged far to the front in this industry when the unfortunate outbreak of hostilities in Europe in 1914 forever terminated the ascendency of Germany in this art. At that time Germany was responsible for more than 75% of the total world production of synthetic dyes, and actually supplied in excess of 90% of all the dyestuffs used in the great textile manufacturing centres of Great Britain. To meet the situation arising from the war, the various foreign governments associated in the prosecution of war against the Central Powers, severally subsidized financially (and aided legally by the seizure of German patents) the formation of dye manufacturing corporations destined eventually to exceed in skill that of the original German manufacturers.

"From a medicinal point of view, the war brought a development of interest in certain of the medical dyes used for the treatment of the enormous number of wounds at the various hostile fronts. From a surgical standpoint this over-interest in medicinal dyes and antiseptics was exceedingly unfortunate. Dyes are the most delicate of chemical weapons against disease, their structure being such that they frequently change in contact with living tissues to so-called leuco dyes. Leuco dyes are colorless. These leuco dyes frequently change into intermediate forms, and then back again to the original dye form. This may easily be demonstrated in the laboratory by bubbling hydrogen sulphide through a cylinder containing a dilute solution of methylene blue. The Methylene Blue is rapidly reduced to the leuco form and the solution becomes colorless. If one wishes now to demonstrate that the dye is still present and has not been permanently changed essentially, one may bubble oxygen through the solution, or one may add an oxidizing agent like ferric chloride, whereupon the color of the methylene blue will rapidly return. This same oxidation-reduction sort of reaction goes on constantly in the body, and is doubtless responsible for some of the medicinal qualities of the dyes. Now materials of such delicate structure are not particularly well adapted to war wounds. The latter are primarily massive injured areas of tissue, deeply contaminated with all kinds of dirt, containing crushed fragments of skin, muscle, tendons, and even bone: and such wounds become secondarily infected. The most efficient antiseptic for that type of wound is surgical cleaning up or debridement. Following that, it frequently is necessary to use chemical materials which dissolve out débris, such as Dakin's Solution.

"Only in cases under very careful hospital conditions would the dyes be particularly applicable. Nevertheless the dyes were widely used during the war and when good results were not obtained, the blame was laid at the door of the dyes rather than the operator employing them.

"The present world dye situation is that there are four important groups competing with each other for world markets. In England there is Imperical Chemical Industries, Ltd., consisting of British Dyestuffs Corporation, Solway, Oliver, Wilkins & Co., and other firms. In Germany there is the great combination known as Interessen Gemeinschaft für Farben Industrie, which contains among others, Badische Anilin; Meister Lucius & Brüning, Baeyer; Cassella; Kalle; and Griescheim Elektron. In France, the great unit has been the Kuhlmann group which has collaborated to a certain extent with the Society of Chemical Industry in Switzerland, with Geigy and others. In the United States, a definite amalgamation of all the chemical companies has neither been legally possible nor commercially desirable. Nevertheless, from scientific and research viewpoints, the work of the American dye companies has been greatly aided by the Chemical Foundation of New York. The great dyestuff manufacturers in this country are DuPont, American Cyanamid, Calco, National Aniline, General Dyestuffs, and several other smaller concerns. If any of you wish to pursue this matter further I refer you to the work by Thorpe on 'Synthetic Dyestuffs,' published by Griffin & Co. of London, from whom I have drawn liberally for the above facts.

"If we may have the slides at this point, I think I can illustrate the nature of each of the dyes, and then go on to a brief discussion of them. The first slide shows the structural formula of Methylene Blue. This is one of the oldest and one of the most interesting of the dyes. Doubtless you have read a great deal in the newspapers concerning the use of Methylene Blue in cyanide poisoning, in illuminating gas poisoning, in carbon monoxide poisoning and in various other conditions. Methylene Blue was proposed as an antidote for such intoxications by Mathilda Brooks and J. C. Geiger, independently, in the West. I have a folder about two inches thick on this subject in my files, but it will suffice to say here what while methylene blue is a moderately good antidote for cyanide poisoning, there are apparently better antidotes. The work of Chen,

Rose and Clowes on nitrites and sodium thiosulphate as well as sodium tetrathionate apparently points the way to more efficient antidotes. For any of you interested in looking up that subject, you will find it in the *Proceedings of the Society for Experimental Biology and Medicine*, Volume 31, page 250, year (1933). Since methylene blue apparently forms meth-hemoglobin when in contact with hemoglobin, it seemed from the first unlikely that it would be useful in carbon monoxide and similar poisoning. This point was well made by Haggard and Greenberg of Yale (*J. A. M. A.*, 100, 2001 (1933)). However, there have been interesting reports by other men, particularly those by Christopherson (*J. A. M. A.*, 100, 25, 2008 (1933)) and Steele and Spink (*New England Journal of Medicine*, 208, 1152 (1933)). We have not heard the last of methylene blue and doubtless scientific investigations now in progress will show some interesting uses for it in medicine, but at the present time it may in emergency be used as 50 cc. of a 1% solution intravenously for cyanide poisoning, and for the ordinary surgical uses. These latter uses are in infected sinuses, in wounds, in injuries and diseases about the mouth, pharynx, gums and accessory sinuses. Methylene blue is locally the mildest, although not necessarily the least toxic of the medicinal dyes in common use. It is a mild bacteriostat. It is ordinarily used in solution of 1 to 1000 or may be used in stronger solutions where particularly indicated. Methylene Blue has some use in malaria, and the recommended dose is 1 Gm. per day by mouth in conjunction with quinine compounds, where it is particularly valued in the treatment of aestivo-autumnal malarial fever. There is one interesting use of methylene blue which deserves some mention. It was first recommended by Blanc in France several years ago as of use in tuberculosis of the bladder. Symptoms from this complication of tuberculosis are extremely annoying to the physician and agonizing to the patient. There is constant pain, and a desire to urinate every few minutes. It is very difficult or impossible to relieve this situation short of curing the tuberculosis. Blanc claimed to have found that methylene blue alleviated the symptoms. Greenberg in this country published within the last couple of years on the subject, and has found excellent results with certain types of methylene blue. He feels that certain so-called impure varieties produce a great deal of irritation and are very much less efficient than other pure varieties. The dose used is 1 grain three times a day, and it may also be used in a solution of 1 to 500 to 1 to 1000 in the bladder. Five cc. of a 1% solution have also been used for instillation into the bladder.

Crystal Violet.—You can see the formula and appearance of the material. So-called Gentian Violet is a mixture of several para rosaniline hydrochlorides. We have particularly sponsored the idea that it would be better to have a dye in this category which is a pure crystalline material and accordingly we have developed and will market the hydrochloride of hexamethylpararosaniline known as Crystal Violet rather than the mixture which has previously been known as Gentian Violet. From a strictly practical point of view there is little clinical difference in the effects of the two. Crystal Violet is of particular interest because it appears to be especially effective against gram-positive bacteria. Such bacteria are staphylococci and to a limited extent streptococci, also the bacillus of diphtheria.

"Accordingly, where an invasion by such organisms is suspected or feared, Crystal Violet is particularly indicated. It is used in strengths of 1 to 500 or 1 to 1000. Where there are a great many staphylococci in the blood stream, the so-called staphylococcic pyaemia, the use of the dye intramuscularly has been recommended. It apparently works in some cases, but I have heard of other cases in which it did not work. There has been an immense amount of interest in the use of Gentian Violet or Crystal Violet in the treatment of severe burns because of the rather startling and originally brilliant work of Aldrich in Boston. I am going to refer to that a little later and show you his own slides.

"*Neutral Acriflavine.*—Acriflavine belongs to the Acridine group of dyes which derive their names from a yellow color. They are chiefly known as Flavines in Europe. The practical usefulness of the group was discovered in 1912 by Ehrlich in the treatment of African trypanosomiasis. Neutral Acriflavine appears to possess marked antiseptic and germicidal properties against some gram-negative and some gram-positive organisms. It has the disadvantage that when taken internally, it appears to be the most toxic of the dyes or at least of those in common use medicinally. Small amounts of it, such as a few grains a day will produce severe nausea and vomiting. It is, however, widely used in infections of the genito-urinary tract, taken by mouth in a dose from $^1/_2$ grain to $1^1/_2$ grains three times a day. The urine must be rendered or maintained alkaline. It appears to be effective in the urine against both gram-negative bacilli, such as

the colon bacillus, and gram-positive cocci. It is occasionally used in wounds in a solution of 1 to 1000 and I understand is used in England for burns.

"Acriflavine has probably been most widely used throughout the world for the treatment of acute, subacute and chronic urethral gonorrhea. It has not only been used by mouth and intravenously, but has been used in solutions of from 1 to 3000 and from 1 to 4000 for direct irrigation of the urethra. I will not debate with you the advisability of irrigation treatments in gonorrhea in the male, but I think in general it is frowned upon except in very expert hands and where there are particular indications therefor. Of course, in the female, it is an entirely different matter.

"*Scarlet Red Sulphonate.*—This material is a complex sodium salt related to beta naphthol. This dye belongs to the group of so-called 'azo' dyes which derive their names from this linkage of two nitrogen atoms which I show you here. Both this material and its congener, Scarlet Red Medicinal Biebrich, have a curious effect of stimulating the growth of the epithelial tissues. Apparently this effect does not extend to other tissues such as fibrous tissues. This material also was greatly abused in surgery both during and subsequent to the war. It must be remembered that any such material must be used only in a clean wound. To attempt to stimulate an infected or contaminated wound would not only be dangerous if you could do it, but fortunately in most cases, you cannot do it. Of course, there are certain exceptions to this rule, particularly the very new technique known as seed implantation of epithelial grafts into infected surfaces, but this is merely the exception that proves the rule. Scarlet Red Sulphonate is slightly soluble in water and more so in alcohol, and thus may be put into solutions in strengths of from 1 to 4% to be applied to clean wounds or the clean edges of wounds for the stimulation of repair. Bettman of Portland, Oregon, has devised a new technique in the use of this material in the promotion of the healing of burns and of skin grafts.

"*Brilliant Green.*—There is little essential difference in the indications for the use of Crystal Violet and those for the use of Brilliant Green. However, Brilliant Green is probably a less efficient bacteriostat and a more efficient stimulant of wound repair. Otherwise, there is little difference and Brilliant Green is very much less used in surgery than Crystal Violet. There has been some new interest in Brilliant Green because of the work of Professor Senin at Nijni Novgorod in Russia. This gentleman has used it in the treatment of sycosis vulgaris, or so-called 'barber's itch.' Technique of his treatment has been to remove all crust and scale with a 5% salicylic ointment and then to lightly brush the areas with a dry sponge, opening them up, and then painting them every day with a 1% alcoholic solution of Brilliant Green and 70% alcohol. The treatment is favorably considered in England.

"*Medicinal Fuchsin.*—This, too, somewhat like Gentian Violet is a mixture of Rosaniline Hydrochloride. It is said to be a mixture of rosaniline and pararosaniline hydrochlorides and its formula is as you see. You are doubtless familiar with the use of Fuchsine and Carbol-Fuchsine as stains for the staining of tuberculosis organisms. I should emphasize here that the medicinal grade of dye is not the grade used for staining in the laboratory, and you should make that distinction to your physician clients if they inquire. Biological stains are standardized according to the methods of the Biological Stain Commission in Washington, and are sold by different firms and subjected to different processes than medicinal dyes. The interest of recent years in Fuchsine has been two-fold. *First*, the interest in its use in athlete's foot, trichophytosis and similar infections. We have recommended particularly a 10% alcoholic solution of basic fuchsine to which has been added 5% aqueous carbolic acid, 1% boric acid and 10% resorcin and 5% acetone. The technique for this may be found in the publication by Tobias (*Journal of the Missouri Medical Assn.*, 27, 443 (1930)). The second very interesting use of fuchsine is in connection with burns. This is as yet unpublished and I shall refer to it later in the section on burns.

"I think I have now given you a rough bird's eye view of the six medicinal dyes in common use, their chemical formulas, their physical characteristics, and appearance, and the chief uses at least in outline form. It might be well at this point to advise you of certain contra-indication which apply not absolutely, but in general, to most medicinal dyes. In the first place, they are apparently not well tolerated by the eye. I cannot give you extensive literature basis for this, but I am fairly certain that one should not employ these dyes in the eye. Of course, there may be an exception where it is necessary to use Scarlet Red Sulphonate in connection with grafts on the lid, but in general their use in the eye is to be avoided. Then, too, dyes of an amount in excess

of 0.5 Gm. should not be injected in solutions into closed cavities such as the pleura, the joints, etc. While it is unlikely that 1/2 Gm. of any dye would produce fatal symptoms, nevertheless, a reasonable precaution is not to inject into closed cavities more than 1/2 Gm. of any dye. Finally, dyes should not be used in contaminated, dirty and crushed wounds, until those wounds have been surgically cleaned-up and put in shape for irrigation and healing. Further, patients, who have been taking large amounts of dyes internally should not be exposed to direct sunlight in places as the West where the rays of the sun are extremely intense. This probably also holds true for mercury 'sun-lamps.'

"And now with your permission, I would like to turn to a subject in which I have been very much interested for about fifteen years. The subject is the treatment of burns involving large areas of the body. You are doubtless familiar with the old-time remedy of carron oil which was smeared upon burns with the greatest abandon, without much effect except to break down the skin and superficial tissues and furnish an excellent feeding ground for all the bacteria present, plus all the bacteria carried in by the carron oil. Since then there has been a steady effort upon the part of surgeons throughout the United States to correlate their information and statistics upon burns and to derive therefrom sound conclusions which indicate the way in which the treatment of burns should be directed. The oldest theory in this regard is that a specific protein arises as the result of the burn process, and that this split-protein exercises a severe depressing effect upon the central nervous system, and upon the cells of the body as a whole, at times inducing ulceration of the gastrointestinal tract, severe shock, prostration, fever, delirium, and in many cases, death. A very logical outgrowth of this theory was the treatment of burns by coagulation of the burned areas. Obviously, if these areas were liberating progressively a toxic protein, coagulation of the area prevented this liberation, and so diminished or entirely eliminated, theoretically, the effects I have enumerated above. This coagulation treatment is now generally known as the tannic acid treatment of burns and was introduced by the late Dr. Davidson at Henry Ford Hospital in Detroit where it is still thought of very favorably. I have not time to-night to give you a full consideration of the facts and fallacies in connection with this theory. It is sufficient to say that certain observers in widely scattered communities have reported excellent results from the tannic acid treatment of burns, and that in competent hands it appears to be useful. In all probability, the theory of a burn protein producing the toxicity of burns is not completely tenable.

"The second theory of importance in regard to burns was that of dehydration or abstraction of water or tissue fluid. This theory was lent considerable color by the known increased viscosity of the blood following a burn, the severe renal symptoms and various other factors clearly indicating not only an abnormal water exchange in the body following a severe burn, but an emergency need of the body for large additional quantities of fluid. Certain investigators felt confident that this dehydration was not a mere temporary concomitant of extensive burns, but was in fact the principal underlying cause of the extremely serious effects seen in severe burns within 24 to 72 hours after such cases were admitted to hospital wards. Accordingly, it was a logical outgrowth of such theory, that the introduction of large amounts of fluid, either as water, or glucose solution, or saline solution, subcutaneously, intravenously, and even intraperitoneally, was in order. These measures gave extraordinarily good results in the immediate mortality of burns, and to that extent bore out the theory. I might say parenthetically that the above adjuvant measures are now routine in every good hospital regardless of what principal treatment may be used and it is likely that the proponents of this theory merely discovered something that was absolutely true about burns but was not the principal factor.

"The third theory to which I alluded above, recently proposed in Boston, is that the intoxication following severe burns is directly the result of infection. Certain investigators in 1932 conceived the idea that all the serious effects observed after 12 hours in burned patients were due to the toxemia resulting from infection of the burned area. Obvious as this theory might appear on the surface, its proof is not easy. The best proof was, as is so frequently the case in surgical conditions, empirical by actual trial and error. Treatment designed solely to eliminate infection in the burned area produced such a surprising result as to lend considerable support to the theory itself. This does not mean that the ordinary surgical precautions of the light tent, heat externally applied, fluids, treatment of shock, etc., should be neglected. However, these workers in Boston have devoted their principal efforts, in addition to these routine surgical efforts, toward the restraint of infection. The original treatment of this kind was to clean up the burned area, treat the

shock, and then place the patient under a so-called 'light tent.' This is simply a cradle covered with a blanket and containing electric lights which shed an even light and temperature upon the patient who, of course, is unclothed. The temperature underneath the cradle is kept regulated to between 88° F. and 90° F. by constant inspection of the thermometer kept hanging therein. The original treatment for the first eight hours was that the patient was sprayed on the burned area by an ordinary vaporizing spray with a 1% solution of Gentian Violet, or as was later used, Crystal Violet. This served to form a light, tough eschar, to prevent oozing and loss of fluids, to keep the area sterile, and not least important, to render the whole area analgesic. After a firm eschar had been formed, the area was sprayed every six hours during the day. There were various surgical refinements which it is unnecessary for me to go into. Suffice it to say that this treatment in competent hands in Boston City Hospital has proved eminently satisfactory not only in the immediate results, but in the eventual results. I have seen these patients up and around the ward in light cotton gowns, seated in chairs, eating their meals in an incredibly brief period of time. The growth of the tissues beneath the eschar has been rapid and excellent. In many cases, skin grafting has either been avoided entirely or reduced to a minimum. It must be borne in mind that neither this treatment nor any other treatment can eliminate the eventual plastic surgery, with all its delicacy and refinements, which becomes necessary following very severe burns of any area of the body. Since this original treatment in Boston, I have had the privilege of collaborating in some of the subsequent work, and have made certain suggestions and furnished certain material for the improvement of the technique. At the present time, we believe that mixtures of dyes, probably Crystal Violet, Acriflavine and Brilliant Green or Fuchsine will be used in place of the original Crystal Violet. This is done to hit the various groups of organisms by the method of a shot-gun charge. If we may now have the slides which Dr. Aldrich has kindly loaned me, I will show some of the results with the original Crystal Violet treatment.

"I must compliment you upon your patience in listening to what must have been a rather technical exposition, on a rather technical subject. It is a little difficult for one in my position to get together a talk which will be of interest in the rather highly technical field involved in our work.

"I trust, however, that I have been able to give you some insight into the interesting possibilities of medicinal dyes and let me assure you that if at any time in the future I can give you additional information, I should be more than pleased to receive your letters and shall do my best to answer them promptly. Again, let me thank you for the courtesy you have extended to me this evening by your invitation to address you and express the hope that I may some time attend some of your other meetings as a listener and not as a speaker."

Following the completion of Dr. Bryce's address considerable discussion ensued with many questions being asked by members in the audience. These were all carefully gone over and Dr. Ballard called for a rising vote of thanks to the speaker.

RUDOLF O. HAUCK, *Secretary.*

PHILADELPHIA.

The January meeting of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in the Temple University School of Pharmacy, January 8, 1935.

The minutes of the previous meeting were read and approved and after an announcement concerning the next meeting, President Barol introduced Dr. James C. Munch as the speaker. His topic concerned "Recent Developments in the Pharmacology of Digitalis."

He began with a history of the drug, stating that Withering did not recognize its effect on the heart. This effect is now believed to be a sedative one rather than tonic. Of the 150 active principles formerly listed only 6 are now recognized as having definite heart action.

Dr. Munch said that about 22 drugs have actions similar to digitalis and discussed the specific actions of Strophanthus, Squill, Adonis, Apocynum and Convallaria. Of these, Adonis has the same potency as Digitalis, Apocynum is twice and Convallaria three times as potent.

He said that at the present time 58 methods have been devised for the assay of Digitalis, the newest using the snail heart and is found to correspond to the one-hour frog method. The toad method used in South Africa, and the pigeon method were also mentioned.

Dr. Munch described work now being done to study the cumulative activity of digitalis-

When the therapeutic dose was administered to a group of cats over a 3-day period, a degeneration of the heart muscle was noted.

Potency and standardization were discussed and a series of lantern slides used to illustrate parts of the lecture.

Before adjournment a general discussion took place regarding such topics as acid and alkaline hydrolysis, preservation of finished products, methods for determining rate of deterioration, the new international digitalis powder standard and the preference for chemical or physiological methods of assay.

E. H. MACLAUGHLIN, *Secretary.*

THE NRA.

Elliott Thurston is of the opinion that no prophet lives who can tell what Congress, more especially the Senate will do, or when it will adjourn, or what will happen to the legislation affecting the codes and, eventually, the Supreme Court will decide. State codes have also been affected by decisions—in Wisconsin 20 codes were nullified by a sweeping decision of Chief Justice Marvin B. Rosenberry on March 5th

Whatever may be said, *pro and con*, the drug code has functioned well and to these officials much credit is due.

NARCOTIC RAIDS.

The Narcotics Bureau has been eminently successful in bringing to court narcotic peddlers and Commissioner H. J. Anslinger is to be congratulated on his success. No class is more deeply interested in legal restriction of the dispensing of narcotics than pharmacists.

A cross section of the misty world of the narcotic peddler and addict is expected by Narcotics Bureau officials to result eventually from the spectacular Nation-wide raid.

AN IMPORTANT DECISION.

The recent injunction granted to Eli Lilly & Co., in its case against the Sunset Drug Company for violation of the Lilly contract price under the California Fair Trade act is doubly important to retailers in that state and other states which may pass similar acts. This decision indicates that contracts through wholesalers are valid under the act.

CANCER CURE VENDOR ESCAPES PROSECUTION: DIES WITH CANCER.

A self-styled cancer specialist of Hastings, Mich., died of cancer on the eve of his prosecution on charges of violating the Federal Food and Drugs Act. His principal medicine, "Mixer's Cancer and Scrofula Syrup," composed of potassium iodide, senna, licorice, yellow dock root, sarsaparilla, wintergreen, glycerin, alcohol and sugar syrup, had for a long time evaded the Federal law, until Food and Drug Inspectors intercepted a shipment to Chicago and based a recent case on it. Even during Mixer's last illness, his office force continued to sell and ship the so-called "cancer cure."

A cyclone damaged the offices of **Secretary Walter D. Adams** of Texas Pharmaceutical Association. **B. G. Edwards,** of Forney, Texas, suffered loss by the destruction of his residence and damage to his store. The storm lasted only about a minute, however, during that time caused much destruction, some injuries, but no loss of life.

Secretary H. W. Ayres, of the Washington State Pharmaceutical Association for the past ten years, has taken a leave of absence until September 1st, in an effort to fully recover his health.

Charles E. Turner, former druggist and Mayor of Dallas, has been designated to handle the finances of the Texas Centennial.

RICHBERG HEADS NRA BOARD.

Donald R. Richberg has been appointed by President Roosevelt as acting chairman of the seven-men NRA board. The appointment is temporary only until the revised NRA act is passed by Congress, Mr. Richberg will continue his duties as director of the emergency council.

EDITORIAL NOTES

UNITED STATES CIVIL SERVICE EXAMINATIONS.

Applications for the positions of chemist, and senior, associate and assistant chemists must be on file with the U. S. Civil Service Commission at Washington, D. C., not later than April 8, 1935.

The entrance salaries range from $2600.00 to $4600.00 a year, less a 3½ per cent retirement deduction.

In each of the grades, separate lists of eligibles will be established in accordance with the specialized qualifications shown by applicants. A number of existing vacancies in the Food and Drug Administration, Department of Agriculture, in all grades will be filled from these examinations, as well as a vacancy in the grade of assistant chemist in the Dental Alloy Laboratory, National Bureau of Standards, Department of Commerce.

Full information may be obtained from the Secretary of the United States Civil Service Board of Examiners at the post-office or custom-house in any city which has a post-office of the first or the second class, or from the United States Civil Service Commission, Washington, D. C.

THE TERCENTENARY OF CHEMISTRY.

"Dr. C. A. Browne, chief of chemical and technological research of the United States Bureau of Chemistry and Soils, has officially established 1635 as the date of the birth of American chemical work. Then John Winthrop, Jr., founded the industries that are now so vital to national defense and form so large a source of national wealth.

"At a tercentenary celebration of the American Chemical Society the memory and the vision of this great colonist will be honored when the history of the birth of chemistry in this country, compiled by Dr. Browne, will be read."

In 1642, the General Court of Massachusetts passed an order to raise and produce materials for making gunpowder. Winthrop planned for the production of salt, glass potash, saltpeter, medicines, alum and other materials.

DRUGS FROM AUTOMATIC MACHINES.

An amendment to the Food and Drugs Act Bill of Australia provides that no person shall (*a*) Install any automatic machine for the sale or supply of any drug or medicine; (*b*) permit any such automatic machine to be installed; (*c*) sell or supply any drug or medicine by means of any automatic machine. "Automatic machine" means any machine or mechanical device used or capable of being used for the purpose of selling or supplying goods without the personal manipulation or attention of the seller or supplier or his servant or agent at the time of the sale or supply. Among the reasons given for the clause were the following: 1. The accessibility of the machines to children and young people. 2. The fact that they provide an uncontrolled means of disposing of dangerous drugs. 3. The danger of manipulation, whereby a noxious drug may be substituted in place of the original packet. 4. The fact that the use of the machines leads to the distribution of habit-forming drugs in small quantities, *e. g.*, three tablets for a penny and twelve for threepence. 5. The difficulty of control under the laws relating to poisons and early closing.

A PLAY BASED ON THE LIFE OF SEMMELWEIS.

In Vienna, a play has been produced with the title, "Dr. Semmelweis," from the pen of Hans Refisch. (See *Journal of the A. M. A.*, February 23, 1935.) "The plot was taken from the life of the immortal physician. The drama deals with his struggles and the misjudgment of him by his colleagues. This drama has been produced only in Vienna, which failed to appreciate Semmelweis, seeing in this benefactor of humanity only a charlatan and driving him away. The play as a literary work is not well done, because it consists of long dialogs and tedious scientific disputes. Nevertheless the audience liked it. The leading literary reviews of western Europe have dealt with it meritoriously." See editorial, JOURNAL A. PH. A., 6, 341 (1917). Also pages 351 and 382 same issue.

The press has reported the finding of twelve pieces of broken pottery on the site of ancient Lachisch (one of the capitals of the Canaanites). Dr. J. L. Starkey, head of the *Wellcome Archaeological Research* Expedition, who found the potsherds, entrusted the task of deciphering the inscriptions to Prof. Torcznyer at Hebrew University of Jerusalem. According to the latter this is a most remarkable find; a remarkable fact is that they appear to be written in ordinary ink.

PERSONAL AND NEWS ITEMS.

Dr. Charles A. Shull, professor of plant physiology at the University of Chicago, lectured before the Graduate College at the University of Iowa, on March 25th, on "Radiation and Life."

Francis P. Garvan, president of the Chemical Foundation and recipient of the Priestley Medal as "the greatest lay patron of chemistry," is honorary chairman of the New York Committee organizing the 300th anniversary of the Chemical Industries celebration. Prof. Arthur W. Hixson of Columbia University is general chairman. Senator Pat Harrison of Mississippi and Representative James W. Wadsworth of New York will be among the speakers at a dinner meeting on April 24th.

President Coffman's biennial message (University of Minnesota) is entitled "Youth and Tomorrow's Education," a presentation of some of the problems which confront universities. The message has been published in booklet form.

Howard B. Lewis, director of the College of Pharmacy of the University of Michigan and Professor of Physiological Chemistry in the Medical School, has been elected a member of the National Board of Medical Examiners of the United States, to succeed the late Professor Otto Folin of Harvard.

Mary Dahlgreen Robinson—of Saint Davids, Pennsylvania, through **Charles E. McCormick,** of Baltimore—has donated two mortars, several old dispensing bottles and a quassia cup—to the American Institute of Pharmacy.

Dean R. C. Wilson, University of Georgia, has addressed the radio audiences on narcotic legislation and unregulated sale of barbituric acid preparations and certain other sedatives and hypnotics.

J. D. Ashmore, of Greenville, has been named president of South Carolina Pharmaceutical Association, succeeding L. E. Bishop, who has removed from the state.

Dean A. O. Mickelsen addressed the members of the North Pacific Dental Alumni Association at their annual meeting which was held at North Pacific College, February 7th–9th. His subject was "Prescription Writing by the Dental Profession." Four hundred and seventy alumni members attended.

American winners of the Nobel awards will be guests of honor at a dinner in the Waldorf-Astoria, April 9th, celebrating the 101st anniversary of the birth of Alfred B. Nobel, Swedish scientist who created the awards.

The Hillebrand award of the Washington branch of the American Chemical Society was presented at the society's annual banquet at the Cosmos Club, March 14th, to Dr. F. D. Rossini of the Bureau of Standards in recognition of fundamental work on the thermochemistry of hydrocarbons and alcohols.

Margaret Cousins has written "Purple Cloud," a story of Bernard Courtois, published in the *Southern Pharmaceutical Journal*.

Dean D. B. R. Johnson, College of Pharmacy, University of Oklahoma, is to be honored with a memorial by members of the faculty and friends.

Gustav Bachman, former secretary of Minnesota Pharmaceutical Association, was presented by members of the organization with a beautiful pen set. The presentation was an interesting part of the program of the annual session of the Association.

OBITUARY.

EZRA J. KENNEDY.

Ezra Joseph Kennedy, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1887, died of heart disease, February 20th, at his home in Rutherford, N. J., aged seventy-five years.

Mr. Kennedy was born in Attica, Ohio, where he received his earlier education; in 1882, he was graduated from the pharmacy department of the University of Michigan. While engaged in retail pharmacy in and near Detroit, he taught pharmacy at the Detroit College of Pharmacy. Later he became associated with the *Pharmaceutical Era*, and when the publication came to New York, Mr. Kennedy took up his residence in New Jersey. He remained with the *Pharmaceutical Era* for more than forty years, until his retirement several years ago.

Surviving are four daughters, Mrs. E. A. Dougherty, Mrs. Herbert Bond and Mrs. W. G. Macomber, of Rutherford; and Mrs. Ralph W. Boyd, of Drumright, Okla.; and two sons, Ezra J. Kennedy, of Rutherford, and Fred H. Kennedy, of Cleveland.

SOCIETIES AND COLLEGES.

COMMITTEES FOR A. PH. A. MEETING.

Dean A. O. Mickelson, of the North Pacific College of Pharmacy, has been named Local Secretary.

The following committees have been named by Harvey J. Donnell, secretary of the North Pacific branch of the A. PH. A.

Convention: L. F. Haack, *Chairman;* Frederick Grill, *Secretary;* F. A. Geue, *Treasurer;* F. C. Felter, Frank Nau, Edgar Stipe, Earl Gunther, all of Portland.

Entertainment: H. J. Frank, *Chairman;* Peyton Hawes, M. C. Kaegi, all of Portland.

Reception: Dean Adolph Ziefle, Corvallis, Ore.

Women's Auxiliary: Mrs. Ralph A. Watson, *Chairman.*

Representatives named in the various Northwest states, include:

Oregon: George W. Steelhammer, Silverton; Ernst T. Stuhr, Corvallis; George C. Blakeley, The Dalles; and Roy A. Perry, Portland.

Washington: Dean C. W. Johnson, Seattle; P. H. Dirstine, Pullman; L. D. Bracken, Charles G. Ajax, Seattle.

California: K. B. Bowerman, San Francisco; Frank E. Mortenson, Los Angeles; T. D. Perkins, San Diego.

Idaho: E. O. Leonard, Pocatello; Charles Carter, Moscow; R. M. Curist, Standpoint.

Montana: C. E. Mollet, Missoula; Emil Starz, Helena; J. L. Kracker, Bozeman.

MEETING OF THE PLANT SCIENCE SEMINAR.

The 13th Annual Meeting of the Plant Science Seminar will be held in Portland, Oregon; time to be fixed, according to a recent announcement by President Frank H. Eby.

For the first time in the history of the Seminar, the Annual Meeting will be held on the Pacific coast and a large attendance is anticipated. Professor E. T. Stuhr of the Oregon State Agricultural College has been appointed local secretary. He has not announced a program but information will appear in the JOURNAL as soon as announcements are made.

All persons interested in drug plants are urged to attend the 1935 Seminar. Complete information may be obtained by directing communications to the secretary of the Seminar, F. J. Bacon, Western Reserve University, Cleveland.

DRUGGISTS' BUSINESS CONFERENCE AT PURDUE.

March 13th and 14th were important dates for retail druggists in Indiana. The fifth annual Druggists' Business Conference was held in the Memorial Union Building on the campus of Purdue University. During these two days, problems of vital importance to druggists were discussed.

This conference is arranged for druggists and their clerks, and is sponsored by the Pharmacy Extension Department. The Indiana Pharmaceutical Association took an important part on the program, and discussed recent legislation as it pertains to the druggist President R. P. Fischelis, of the A. PH. A. was an honored guest speaker.

A "one-act play" was given March 13th, at 8:00 P.M., following the dinner and evening address at 6:30 P.M. The occasion honored Dean C. B. Jordan upon the completion of twenty-five years of distinctive service as dean of Purdue University School of Pharmacy.

BI-CENTENNIAL OF THE ACADEMY OF MEDICINE, MADRID.

The Academia Nacional de Medicina of Madrid celebrated recently its second centennial. The festivities included several meetings during the medical week and an exhibition of the books of the library, which has, among other books of great importance, the Codex scientiæ medicinæ of Avicenna, in five large volumes, and a collection of books written by Hipolito Ruix on American plants, which for more than three centuries were a source of information for botanists and designers from all over the world.

IOWA.

The annual election of officers of Iowa Pharmaceutical Association resulted as follows: *Honorary President,* J. F. Shuey, Jefferson; *President,* W. H. McClelland, Corning; *First Vice-President,* R. J. Allen, Sioux City; *Second Vice-President,* A. E. Thomas, Des Moines; *Third Vice-President,* George McShane, Waterloo; *Treasurer,* J. M. Lindly, Winfield.

Members of the Legislative Committee: George Judisch, Ames; George W. Gillman, Ft. Dodge; T. H. Kenefick, Eagle Grove; J. J. Gillespie, Des Moines; W. F. Meads, Des Moines.

Among the visitors were Secretary John W. Dargavel, of the N. A. R. D.; Guy Butler, Lincoln, president of the Nebraska association; J. G. McBride, secretary of the Nebraska association; Otto A. Kuether, Herington, president of the Kansas association; W. M. Newmark, Topeka, secretary of the Kansas association; W. H. Varnum, Lawrence, treasurer of the Kansas association and secretary of the Midwest Conference; Coleman Dais, Seminole, president of the Oklahoma association; A. Roy F. Johnson and F. G. Kustermann of the Minnesota association; J. P. Jelinek, president of the Northwest Pharmaceutical Bureau and J. R. Bruce and Frank M. McCabe of *North Western Druggist.*

F. W. Fitch, Des Moines, has completed an analysis of the price stabilization situation within the drug industry and with the assistance of his attorneys has worked out a plan which he believes is both simple and practical.

The plan is based on the filing and registration with each secretary of state the manufacturer's trade-mark and resale price. Briefly, this means that in each state the manufacturer would file his trade-mark and resale price under a law making it a violation for anyone to sell trade-marked merchandise at any other price than that filed with the Secretary of State.

According to the proposer's belief the plan is advantageous to the manufacturer in that it would mean just one operation in each state instead of contracting with several thousand druggists in each state. He contends it should be easy of enforcement because it is a state statute, instead of a violation of a contract between individuals.

NORTHWEST PHARMACEUTICAL BUREAU.

At the annual conference dinner of the Northwest Pharmaceutical Bureau in Des Moines, February 20th, President John P. Jelinek of St. Paul, stated that the organization through its annual Great Northwest Drug Show had turned into the Northwest association treasuries almost $40,000.00 during its years of existence.

The following officers were elected: *President,* James J. Gillespie, Des Moines; *Vice-President,* Fred G. Kustermann, St. Paul; *Treasurer,* Robert M. Gibson, Des Moines; *Secretary,* N. Vere Sanders, Albert Lea; *Executive Committeemen:* Otto A. Bjornstad, Spencer, Ia.; John P. Jelinek, St. Paul, Minn.; Edward J. Boberg, Eau Claire, Wis.; Homer L. Hill, Towner, No. Dak.; Fred L. Vilas, Pierre, So. Dak.; *Committeeman-at-large,* E. L. Beezley, Cedar Rapids, Ia.

NORTH DAKOTA.

The fiftieth annual convention of the North Dakota Pharmaceutical Association will be held in Fargo, June 11th, 12th and 13th.

WISCONSIN.

Ralph W. Clark reports that the first mid-winter conference, held by the Wisconsin Pharmaceutical Association, February 27th, was well attended and conceded by all to be a great success. Over three hundred druggists came to this business session fully realizing the seriousness of the present times as far as independent merchants are concerned. They showed their willingness to follow the able guidance of their officers and legal counsel and most certainly will coöperate with them throughout the present legislative session.

Attorney Mount, Milwaukee, counsel for the Wisconsin Pharmaceutical Association, explained the proposed legislation, the Wisconsin Fair Trade Practices Act, which has been introduced into the Assembly. This legislative body arranged an informal committee hearing on the bill which was attended by the druggists and others representing independent merchants' organizations.

MINNESOTA.

Conforming to the usual program a session of Minnesota Pharmaceutical Association was devoted to the Scientific and Practical Section under the chairmanship of Dean Frederick J. Wulling. Among the many papers presented were "Plants and Their Relation to Man," by Gustav J. DeMars; "The Open Prescription Department," by President Theodore A. Arneson; "British Pharmaceutical Codex," by F. A. Upsher Smith; "The Operation of a Hospital Pharmacy" by Sister St. George and a most comprehensive and interesting report by the retiring secretary, Gustav Bachman. The section included, also, many other interesting papers of scientific importance.

Although illness depleted the official ranks of the Minnesota State Pharmaceutical Association during the organization's convention in St. Paul the week of February 26th, the meeting was highly successful from every viewpoint, ushering in a second half-century of service to its members with renewed enthusiasm and determination.

MINNESOTA NOMINEES.

The following are nominees for the Minnesota association offices—to be voted upon by mail—ballots to be transmitted to members by mail: *President*, R. G. Paulson, Fairmont; Wilford J. Schwankl, Sauk Rapids. *First Vice-President*, Jesse B. Slocumb, St. Paul; William Shepard, Minneapolis. *Second Vice-President*, Orlando Didra, Waseca; Margaret Armitage, Princeton. *Third Vice-President*, L. M. Herbert, Worthington; Guy Hovland, Dawson. *Secretary*, A. Roy F. Johnson, Minneapolis; Harry J. Anderson, North Branch. *Treasurer*, C. T. Heller, Jr., St. Paul; B. J. Witte, Jr., Anoka. *Executive Committee:* Joseph Vadheim, Tyler; H. O Tiegen, Moorhead.

LEGAL AND LEGISLATIVE.

PROFESSIONAL EMPLOYEES.

Professional persons in the retail trade working unlimited hours are entitled to the same minimum wage classifications as executives working beyond code hours under an amendment to Article V, Section 4 (*a*) of the retail trade code, approved by the National Industrial Recovery Board, it was announced January 3rd.

Article V, Section 4 (*c*) of the code provides that executives who work unlimited hours must receive minimum wages ranging from $25.00 to $35.00 a week, according to population of the communities in which a retail establishment is located.

The term "professional person" is defined in the code. It includes, but without limitation, such employees as doctors, dentists, nurses, architects, training directors, artists, research technicians, statisticians, mechanical engineers, etc.

CODE AUTHORITIES GRANTED EXEMPTION FROM INCOME TAX.

Under a ruling of the Commissioner of Internal Revenue announced March 13, code authorities are entitled to exemption from Federal Income taxes and from filing returns therefor.

They are required, however, to file with the Collector of Internal Revenue in their district an affidavit in the form required by Article 101-1 of Regulation 86 of the Bureau of Internal Revenue, setting forth the character of the organization, the purpose for which organized, its activities, the sources and disposition of its income, whether any of its income is credited to surplus or may inure to the benefit of any private individual and all other general facts relating to its operations which bear upon its right to exemption as a non-profit entity.

The exemption does not extend to members or employees of code authorities as individuals.

POSTPONE EFFECTIVE DATE OF ORDER RESTORING SALES OF TOILET SOAP TO RETAIL CODE JURISDICTION.

The National Industrial Recovery Board on March 12th, announced that the effective date of the order making sales of toilet soap again subject to the retail drug code loss limitation provision has been extended to April 5, 1935.

Sales of toilet soap were placed under a loss limitation provision similar to that of the retail food and grocery trade code (cost plus 6 per cent), but an order approved February 19th, effective in 21 days, was issued to restore such sales to the retail drug trade code provision. Considerable confusion has arisen, however, and it has been deemed advisable to prepare an order suspending the loss limitation provision of the retail drug code in so far as toilet soap sales are concerned.

In order to permit a decision on such an order, the effective date of the February 19th order has been extended to April 5th.

SALES TAX.

Texas and Kansas oppose a sales tax. New York, Michigan, Colorado, West Virginia, South Dakota, Washington, California, Wyoming, Montana, Maine and Connecticut have sales tax provisions. Arkansas, Tennessee, Massachusetts, New Jersey, Indiana, Wisconsin are considering measures. The West Virginia law expires July 1st, but the Governor has been asked to extend the time. **(Texas is now considering a sales tax.)**

HEARINGS ON THE COPELAND BILL.

Hearings were held on the Copeland Bill S. 5 (Committee Print No. 3) March 2nd and 8th, before members of the Sub-Committee of the Committee on Commerce of the Senate, of the United States, Senator Clark of Missouri, *Chairman*.

Representatives of interested associations and organizations attended and about seventy witnesses were scheduled for the hearings. There was some heated discussion and differences of opinion obtained, evidencing deep interest—it proves what Dr. Carl L. Alsberg stated several years ago, that "In appraising legislation intended to protect public health or prevent fraud, it is not enough to inquire whether the abuses aimed at are likely to be cured. Political and social consequences need to be envisaged also."

No effort is made to submit opinions on what the Food and Drugs Act should be nor analyze the testimony given. The committee heard many views and, perhaps, enough for reaching conclusions as to what form the presentation in Congress should take. When the measure comes up for action there will, probably, not be unanimity but compromise on some of the stronger contentions. There are some differences of opinion among those to whom the law applies and also among those who frame it and enact the measure.

ARKANSAS.

The Arkansas Legislature has passed a bill to prohibit the sale of barbituric acid or derivatives and compounds thereof under any copyrighted or chemical names, except to wholesale drug houses, chemical houses and dispensing pharmacies or practicing physicians, providing that these may not be dispensed except by a practicing physician or retail pharmacy on prescription written by a physician.

IDAHO.

Idaho pharmacists are making a determined effort to put pharmacy's affairs again in the hands of pharmacy. A new pharmacy bill (H. B. 67) takes pharmacy control out of the Department of Law Enforcement under which it has been for many years, and puts control in the hands of a state board of pharmacy. This bill passed the house by a vote of 51 to 6 and is said to have the approval of the Governor. This bill will, if passed, create an entirely new set-up for pharmacy in Idaho. It provides that the new board of pharmacy shall be elected by the state association which will then meet in Boise in June to elect members to the new board and interpret the other provisions of the law for the benefit of Idaho druggists.

MARYLAND.

Three bills regulating the drug industry were considered by the Hygiene Committee and referred to the House of Delegates on March 8th.

One measure provides that the United States Pharmacopœia and the National Formulary shall be on file at all times in every pharmacy; that every registered drug store keep a certain minimum of utensils and maintain sanitary standards; that prescription records be filed and that all medicines and drugs be open for inspection at all times wherever they are manufactured or sold.

Another requires that all pharmacies and manufacturers of drugs, medicines, dentifrices, toilet articles and cosmetics shall secure permits from the Maryland Board of Pharmacy.

The third measure would regulate the sale of barbital compounds by making their sale legal only on prescription.

MINNESOTA.

A Minnesota bill provides for the regulation of the practice of pharmacy—the sale of drugs, medicines, chemicals, poisons; the establishment of a State board of pharmacy and defining its powers and duties; requirements for registration, licensing pharmacies and pharmacists, etc.

OREGON.

The new Oregon pharmacy law is patterned largely after the model pharmacy law sponsored by the National Association of Boards of Pharmacy. It gives more power to the state board in its regulation of pharmacy; provides for registration of all pharmacies with an annual registration fee of $3.00; provides for elimination, after a few years, of the assistant classification; governs more strictly the sale of poisons and of denatured alcohol; sets up a license for non-pharmacy outlets who sell medicinal products; restricts use of such words as "drugs," "druggist," "pharmacy," etc., on signs and in advertising to stores where registered pharmacists are employed; sets new fees for registration by examination or reciprocity and provides certain library and equipment requirements for pharmacies. These are a few of the more important new provisions.

(*Continued on page 255.*)

LEGAL AND LEGISLATIVE.—*Concluded from page 254.*

NARCOTIC RULES FOR VIRGIN ISLANDS REVISED.

An executive order by the President has promulgated revised rules governing narcotics in the Virgin Islands. Narcotics must be obtained from qualified manufacturers or wholesalers in the continental United States. The regulations that apply follow:

Article 81. *Orders—Who May Fill.*—An order for narcotic drugs submitted by a qualified dealer or practitioner in the Virgin Islands in accordance with the terms of the executive order may be filled only by a person duly registered, in the continental United States, in Classes 1 or 2 under Section 1 of the Harrison narcotic law, as amended, and regulations issued thereunder, except that an order for only such preparations and remedies as are considered exempt under Section 6 of said law and regulations issued thereunder may be filled by a person duly registered, in the continental United States, in Class 5 under Section 1 of said law and regulations.

Article 82. *Record and Report of Sales.*—Each sale or other disposition of narcotic drugs under the executive order shall be recorded and reported as a domestic sale, and the person filling any such order for narcotic drugs shall enter upon form 810*b* or 811*b*, as the case may be, of his monthly return the date upon which the order was approved by the commissioner of health of the Virgin Islands, in lieu of and in the space provided for the date of the purchaser's official order form. The column headed "Serial number" should be used for inserting the date of receipt of the purchaser's approved order. The columns headed "Registry number," "Class" and "District" will be left blank. If the order covers items of preparations or remedies which are considered exempt under Section 6 of said law and regulations, such items will not be reported in the monthly return, but the person filling the order for such items shall keep a record in the same manner as in the case of a domestic sale thereof, except that in lieu of the record required to be kept of the registry number of the purchaser there shall be kept a record of the date upon which the order was approved by the commissioner of health of the Virgin Islands and the date when the order was received by the person in the continental United States filling the order.—From *Oil, Paint and Drug Reporter*, Feb. 18, 1935.

CALIFORNIA.

HYDROGEN PEROXIDE A DRUG OR MEDICINE.

A manager of a pharmacy was charged with violating Section 13 of the California pharmacy practice act in that he permitted named persons, who were not registered pharmacists or assistant pharmacists, to sell peroxide of hydrogen. He was found guilty in the trial court and appealed to the appellate department, superior court, Los Angeles County, California.

Section 13 of the pharmacy practice act makes it unlawful for any "proprietor" of a pharmacy to permit the sales of drugs, medicines or poisons by anyone except a registered pharmacist or assistant pharmacist. The defendant contended that since he was not a "proprietor" but a "manager," his conviction was unwarranted. The superior court held, however, that a mere statement in the charge that the facts alleged constituted a violation of one section of the pharmacy practice act did not prevent the court from upholding the conviction if the acts charged were prohibited by any other section.

The defendant also argued that peroxide of hydrogen is not a drug or medicine within the meaning of the pharmacy practice act. We are satisfied, said the court, that "drug or medicine" are broad enough to include peroxide of hydrogen. It is a well-known chemical substance, listed in the United States Pharmacopœia and described in all encyclopedias.

The court stated that there "may be some difficulty in applying the pharmacy practice act to substances which have both a medical and a non-medical use," but in the case of peroxide of hydrogen we are aided by the provisions of Section 16, of the act, which provides, by way of exception to the general provision of the act, that permits may be issued for the sale by unregistered persons in the rural districts of "simple household remedies and drugs," among which is listed peroxide of hydrogen. Such an exception gives rise to a strong implication that if excepted would otherwise have been within the purview of the act.

The judgment of conviction was affirmed. People *vs.* Arthur (Calif.), 32 P. (2*d*) 1002.—Through *Journal A. M. A.*

NATIONAL TUBERCULOSIS ASSOCIATION.

As the major educational effort of the affiliated tuberculosis associations of the United States during 1935 will launch an Early Diagnosis Campaign on April 1st. Under the slogan "Fight Tuberculosis with Modern Weapons" the need will be emphasized for prompt treatment of tuberculosis when a case is discovered and shall endeavor to familiarize the public with improvements in treatment during recent years that have greatly increased the chances for cure.

NOTICE TO CONTRIBUTORS TO THE JOURNAL AMERICAN PHARMACEUTICAL ASSOCIATION.

The following notice has been prepared from comments received from members of the Board of Review of Papers and of the Publication Committee.

Manuscripts should be sent to Editor E. G. Eberle, 2215 Constitution Ave., N. W., Washington, D. C.

All manuscripts should be typewritten in double spacing on one side of paper $8^1/_2$ x 11 inches, and should be mailed in a flat package—not rolled. The original (*not* carbon) copy should be sent. The original drawings, not photographs of drawings, should accompany the manuscript. Authors should indicate on the manuscript the approximate position of text figures. All drawings should be marked with the author's name and address.

A condensed title running page headline, not to exceed thirty-five letters, should be given on a separate sheet and placed at the beginning of each article.

The method of stating the laboratory in which the work is done should be uniform and placed as a footnote at end of first page, giving Department, School or College. The date when received for publication should be given.

Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperature (for example: 2 Kg., 1 inch, 20.5 cc., 300° C.). Spell out all indefinite and approximate periods of time and other numerals which are used in a general manner (for example: one hundred years ago, about two and one-half hours, seven times).

Standard abbreviations should be used whenever weights and measures are given in the metric system, *e. g.*, 10 Kg., 2.25 cc., etc. The forms to be used are: cc., Kg., mg., mm., L. and M.

Figures should be numbered from 1 up, beginning with the text-figures (line engravings are always treated as text-figures and should be designed as such) and continuing through the plates. The reduction desired should be clearly indicated on the margin of the drawing. All drawings should be made with India ink, preferably on white tracing paper or cloth. If coördinate paper is used, a blue-lined paper must be chosen. Usually it is desirable to ink in the large squares so that the curves can be more easily read. Lettering should be plain and large enough to reproduce well when the drawing is reduced to the width of a printed page (usually about 4 inches). Photographs intended for half-tone reproduction should be securely mounted with colorless paste.

"Figure" should be spelled out at the beginning of a sentence; elsewhere it is abbreviated to "Fig.;" per cent—2 words.

The expense for a limited number of figures and plates will be borne by the JOURNAL; expense for cuts in excess of this number must be defrayed by the author.

References to the literature cited should be grouped at the end of the manuscript under the *References*. The citations should be numbered consecutively in the order of their appearance (their location in the text should be indicated by full-sized figures included in parentheses). The sequence followed in the citations should be: Author's name (with initials), name of publication, volume number, page number and the date in parentheses. Abbreviations for journals should conform to the style of *Chemical Abstracts*, published by the American Chemical Society.

(1) Author, A. Y., *Am. J. Physiol.*, 79, 289 (1927).

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The Editor will appreciate comments from Board of Review and Committee on Publication, members, authors and others interested.